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Original Communications

CHRONIC AURICULAR TACHYCARDIA WITH UNUSUAL RESPONSE TO CHANGE IN POSTURE

REPORT OF TWO CASES

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FINE and Miller,[1] in 1940, presented a bizarre case in which, over a period of several years, so-called "paroxysmal" auricular tachycardia was invariably present as long as the patient sat or stood erect, and more often than not also persisted during recumbency. The rate of the tachycardia varied markedly on change of position. Shortly after this report was submitted, a second case, which was strikingly similar in most respects to the previous one, came to our attention at the Newark Health Department. The coincidence of observing concurrently these two cases of a chronic form of auricular tachycardia with unusual response to change of posture leads us to believe that this condition may not be unique, but that similar cases may have escaped recognition.

In the present communication we shall review both cases in detail, and attempt to delineate the symptom complex which distinguishes them.

CASE REPORTS

CASE 1.*—O. H., a 16-year-old white schoolgirl, was referred to the Cardiac Clinic in October, 1937, because of tachycardia. Since 1931 she had experienced recurrent attacks of pain and swelling of the joints of unknown cause. The knee, elbow, and wrist joints were involved symmetrically. In July, 1935, she was found to have prenatal syphilis, and appropriate therapy was instituted. The chief complaint was abnormal fatigability. There were but slight dyspnea and palpitation on unusual exertion or excitement. For several years she had noticed weakness, dizziness, and, occasionally, syncope upon standing erect. These symptoms were particularly annoying when she arose from bed after a sleep. She practically never perspired, and was greatly distressed by hot weather. The menses were scant and irregular, and were accompanied by moderately severe dysmenorrhea.

Her father was suffering from syphilis and pernicious anemia. Her mother and sister also had syphilis. A brother died of acute appendicitis.

Physical Examination.—The patient was a fairly well-developed adolescent girl of average intelligence. She weighed 104 pounds and was

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*This case has been reported previously.[1] The history and physical signs are herein reprinted almost verbatim.

58.5 inches tall. There was no abnormal pigmentation of the skin or mucous membranes. The pupils were irregular, unequal, slightly dilated, and reacted sluggishly to light. The upper central incisors were typical Hutchinson's teeth. The tonsils were not obviously diseased. The thyroid gland was not enlarged. The thoracic contour and the lungs were normal. The apex beat was within normal limits. No thrills or abnormal pulsations were present. The heart rate (seated) was 180 per minute, and the beating was regular. The heart sounds were normal at the apex, but the pulmonic second sound was split. No murmurs were audible. The blood pressure was 80/60. No abdominal organs or masses were palpable. The knee jerks were hyperactive.

Laboratory Data.—There were no abnormalities in the blood cell count or in the urinalysis. The blood sugar level was 80 mg. per 100 c.c., and the blood urea was 14 mg. per 100 cubic centimeters. The blood Wassermann reaction was strongly positive (4 plus). Examination of the spinal fluid gave the following results: Wassermann reaction, anticomplementary; globulin, positive; cell count, 7; colloidal gold curve, 5555320000. On three occasions the basal metabolic rate was –25 per cent, –26 per cent, and – 13 per cent, respectively. The Mantoux tuberculin reaction was negative with 0.1 c.c. of 1:100 O.T. The vital capacity was normal (2,900 c.c.). A teleroentgenogram showed a hypoplastic type of heart. Roentgenograms of the knee joints showed nothing abnormal.

Additional Cardiovascular Studies.—Over a period of observation of six years the patient had a tachycardia which was invariably present when she was in the sitting and standing postures and frequently in the supine position. Of particular interest was the fact that the rate of the tachycardia varied with change in posture. For example, the pulse rate was usually about 120 per minute in the recumbent position, 150 in the sitting, and 180 in the standing. The range in pulse rate in the recumbent position was 80 to 140, in the sitting, from 108 to 180, and, in the standing, from 136 to 200 per minute. The difference between the recumbent and standing rates was never less than 40 beats per minute, and the rate in the sitting position was usually about the mean of the other two.

The heartbeat was always regular when she was in the erect posture. Rarely, dropped beats were noted when she was in the sitting position. The heartbeat was most often irregular during recumbency. Elevation of the foot of the bed accentuated the irregularity and retarded the pulse rate.

The change in pulse rate when the patient passed from the horizontal to the vertical position was instantaneous. When she changed from the vertical to the horizontal, however, the alteration in rate was sometimes abrupt and sometimes gradual. The pulse rate was accelerated by exercise only on the rare occasions when the rate in the erect posture was below 150 per minute. The application of oculobulbar or carotid sinus pressure did not retard the pulse rate or restore normal rhythm. There was no response to the Valsalva experiment.

It was possible, by administering digitalis or quinidine, to maintain the pulse rate at a normal level, i.e., about 90 per minute in the supine, and 96 in the standing, position, and to eliminate orthostatic symptoms. The blood pressure was usually between 90 and 100 mm. Hg, systolic, and 60 and 75, diastolic. Its postural variations, however, were within normal limits. The blood pressure was not significantly altered by digitalis or quinidine. The application of a tight abdominal binder did not influence the blood pressure or pulse rate.

Subsequent Course.—Due to the fact that the abnormalities of the spinal fluid persisted despite intensive antisyphilitic therapy, the patient was referred to the Greystone Park State Hospital for malarial therapy on June 21, 1943. The diagnosis was syphilitic meningoencephalitis, without psychosis. The patient was digitalized before and

during treatment. Malarial therapy was started on June 30 by inoculation with tertian malaria. She experienced eight chills. The pulse rate during the height of the fever varied from 78 to 146 per minute, and the pulse was of good quality. During her eighth chill the patient got out of bed suddenly, became weak and cyanotic, and fell unconscious. She died shortly afterwards, on July 19, 1943. Necropsy was not done.

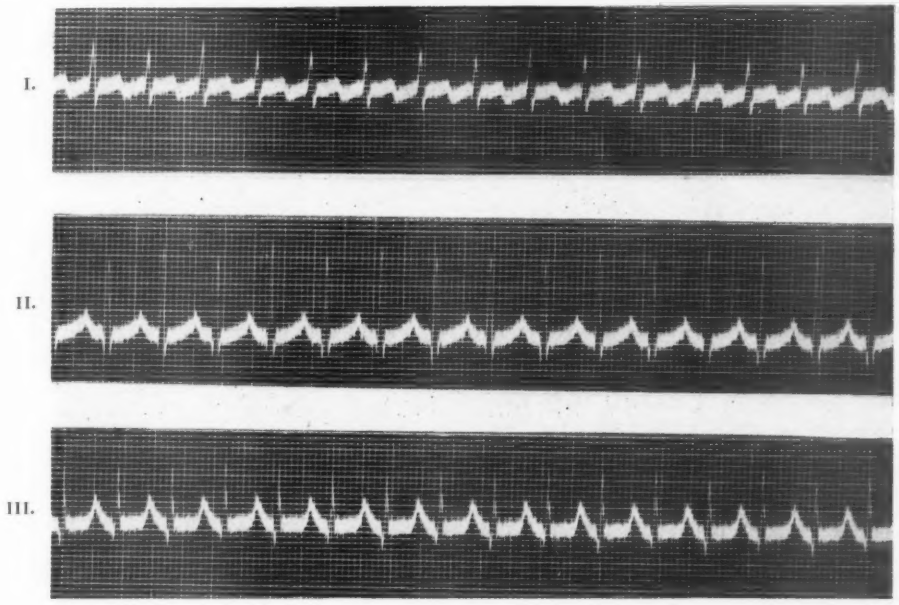

Fig. 1.—Case 1. Electrocardiograms taken Aug. 28, 1942, with patient in erect posture. Auricular tachycardia: rate 166 per minute. P_1 inverted, P_2 and P_3 upright. P-R interval about 0.16 second. Electrical alternation of R_1, S_1, Q_2, R_2, and Q_3.

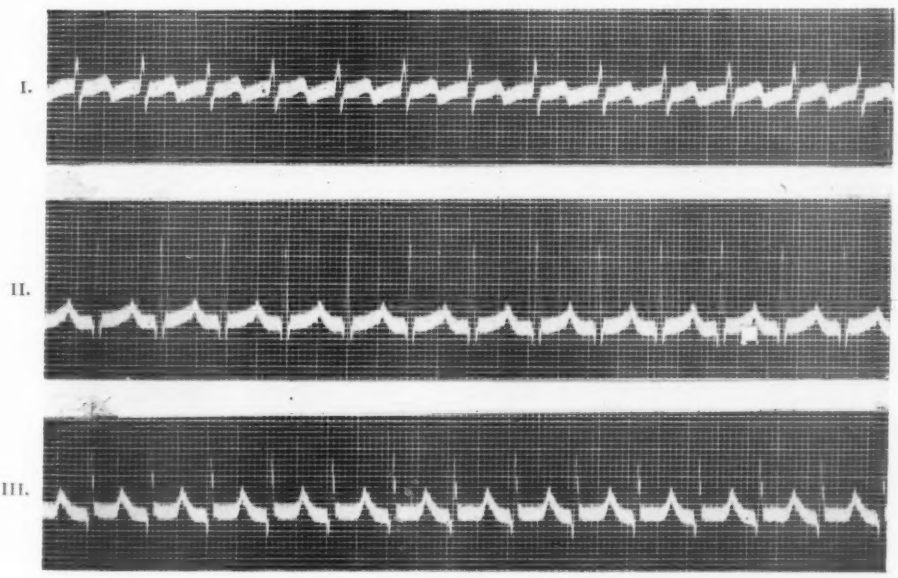

Fig. 2.—Sitting position, taken immediately after Fig. 1. Rate slower, about 139 per minute. P-R interval longer, about 0.20 second.

Analysis of Electrocardiograms.—Electrocardiograms which were taken on eleven occasions invariably showed orthostatic auricular tachycardia which changed rate on change of position. In the supine position there was either normal sinus rhythm, or, more frequently, auricular

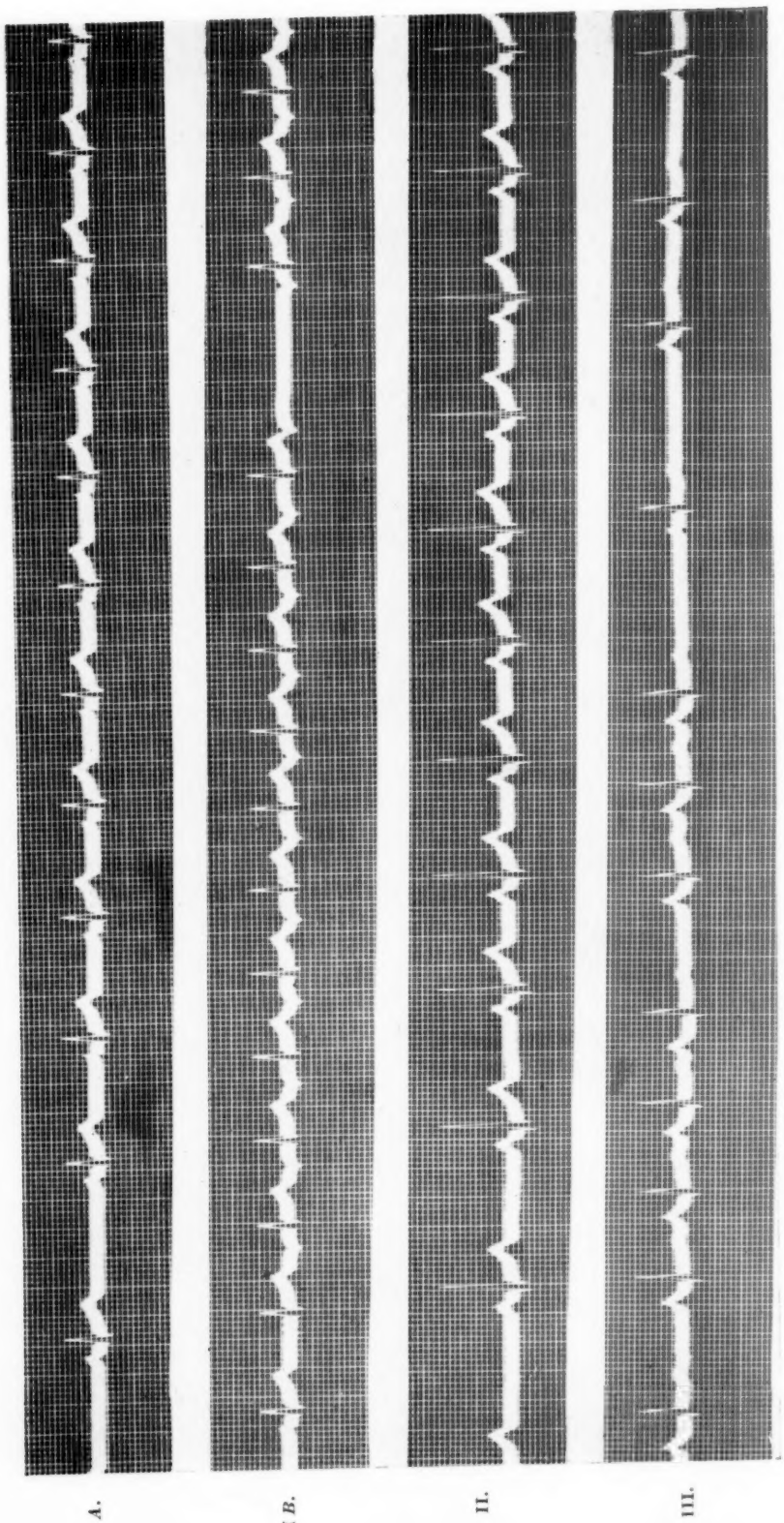

Fig. 3.—Supine position, immediately after Fig. 2. First two strips, Lead I, between which twenty cycles similar to last cycle of strip *A* and first cycle of strip *B* have been deleted. First two beats of sinus nodal origin. Following sequence of beats originated in lower center in sinus node. Second P wave of strip *B* is a transitional complex. Third beat of strip *B* inaugurates an ectopic rhythm with progressive increase in P-R interval. Eleventh beat of this run is blocked, and, following a pause, the ectopic center resumes command of the heart. Lead II, sinus bradycardia and shifting pacemaker. Lead III, short runs of auricular tachycardia.

tachycardia. During the tachycardia in the latter position when the rate was comparatively rapid, incomplete A-V block with the Wenckebach phenomenon was often noted. The electrocardiograms in Figs. 1, 2, and 3 are presented for more detailed analysis; they were taken Aug. 28, 1942, in the standing, sitting, and supine positions.

In the standing position (Fig. 1) paroxysmal tachycardia was present at a fairly constant rate of 166 per minute. The P wave was inverted in Lead I and upright in Leads II and III. The ectopic focus, therefore, was thought to be located in the left auricle.[2] Electrical alternation of the QRS complexes was noted in all leads. The P-R interval could not be measured accurately because the first portion of the auricular deflection was superimposed upon the preceding T wave. It was estimated at approximately 0.16 second.

In the sitting position (Fig. 2, taken immediately after Fig. 1) the auricular tachycardia persisted, but at a slower rate, i.e., about 139 per minute. The P waves differed very slightly in contour from those in the vertical position. This variation was ascribed to change in the electrical axis of the auricles with change in position, rather than to a shift of the ectopic focus. The P-R interval was longer than that in the preceding position. It was estimated at about 0.20 second.

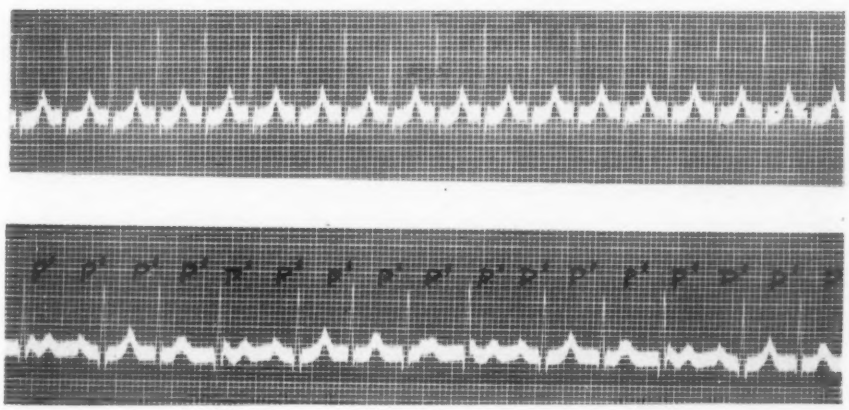

Fig. 4.—Oct. 13, 1939. Lead II. Upper tracing, patient standing. Auricular tachycardia, rate 176 per minute. Lower tracing, immediately afterwards, patient lying down. Auricular rate 170 per minute, incomplete A-V block with Wenckebach periods.

The electrocardiograms in the supine position (Fig. 3, recorded immediately after the preceding figure) were of special interest. In Lead I the first two beats were in response to the normal sinus pacemaker. The P wave was upright and of normal configuration, and the P-R interval was 0.16 second. The R-R cycle was 1.21 seconds in duration, corresponding to a heart rate of 50 per minute. After the second beat there was a shift to a secondary pacemaker lower down in the sinus node. The P wave which originated in this focus was lower in voltage, shorter in duration, and more sharply peaked than the normal. There was no change in the P-R interval. The rate was faster, about 74 per minute, and there was slight sinus arrhythmia. The wandering of the pacemaker in this instance must be ascribed to an enhanced irritability of the lower nomotopic center, rather than to a vagal effect, which is characterized by a decrease in the heart rate as the pacemaker descends toward the A-V node. There ensued a series of thirty-one beats from this focus, twenty of which have been deleted between strips *A* and *B* of Lead I. The second auricular complex in strip *B* was probably a transitional beat. The third auricular complex was inverted, and therefore ectopic in origin. It inaugurated a short run of paroxysmal tachycardia, at a rate of 107 per minute. The last auricular impulse of this

run was blocked, and, after a pause of one second, the ectopic focus resumed command of the heart. This is a decidedly unusual occurrence in the course of paroxysmal auricular tachycardia, and will be commented upon later. Leads II and III showed a wandering pacemaker (shifting possibly to an ectopic focus) and, in addition, in Lead III, there were short runs of tachycardia.

Fig. 4 is presented in order to demonstrate A-V block with Wenckebach periods during auricular tachycardia at a fast rate in the supine position.

Fig. 5 shows auricular tachycardia at a comparatively slow rate, about 100 per minute in the supine position, without A-V block.

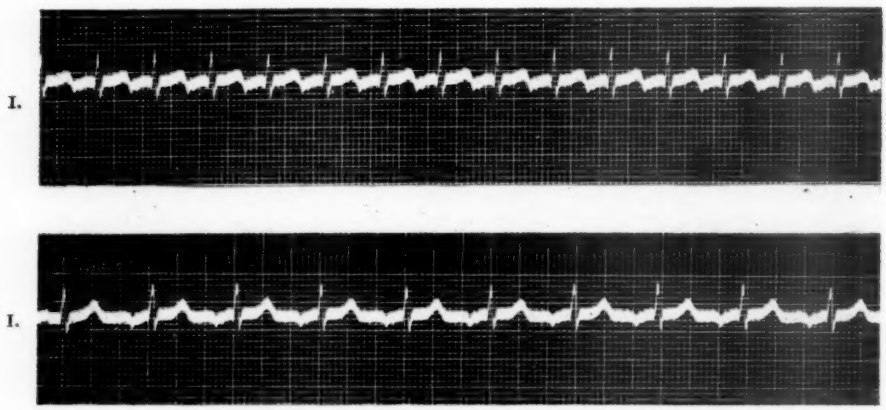

Fig. 5.—Dec. 14, 1940. Lead I. Upper tracing, standing position. Auricular tachycardia, rate 166 per minute. Lower tracing, immediately following, patient supine. Rate about 100 per minute, no A-V block.

Comment on Case 1.—This patient suffered moderate disability as a result of her persistent orthostatic tachycardia. It is possible that the tachycardia was a contributory cause of her death during malarial therapy. It is of interest that she exhibited many of the cardinal features of the syndrome of idiopathic orthostatic hypotension, as set forth by Bradbury and Eggleston,[3] namely, orthostatic dizziness and syncope, abnormal fatigability, hypophidrosis, intolerance to heat, and a low basal metabolic rate. Indeed, the history suggested that this case might be an example of orthostatic hypotension, and led to investigation of the dynamics of the circulation in the various postures. It was a distinct surprise to discover that the underlying cause of her symptom complex was auricular tachycardia. It was of interest that, when the auricular tachycardia was held in abeyance by digitalis therapy, the postural variations in pulse rate were within normal limits and her symptoms disappeared. We may conclude, therefore, that this case was not primarily one of an orthostatic defect in venous return, but that the venous return was deficient only when the pulse rate was excessively rapid during the progress of the auricular tachycardia.

Case 2.—C. M. R., a Negro girl, 14 years of age, was referred to the Cardiac Clinic of the Newark Health Department in November, 1940, for study because of tachycardia which was first discovered by her school nurse. She presented no complaints, and had been indulging in athletics without disability. Sweating and heat tolerance were normal. Aside from attacks of measles, mumps, and chicken pox in childhood, she had always been perfectly well. The menarche had occurred at the

age of 13 years, and her periods were normal. Her father had died of cerebral hemorrhage at the age of 61 years, and her mother had died of pneumonia. Five brothers and one sister were living and well.

Physical Examination.—The patient was well developed, of hypersthenic habitus, and slightly overweight. She was 61 inches in height, and weighed 132 pounds. She was intelligent, cooperative, and phlegmatic in disposition. The skin and mucous membranes were clear. Her teeth were in good repair, but her tonsils were hypertrophied and diseased. The thyroid gland was not enlarged. The thoracic contour was symmetrical. The lungs were normal. The heart was of normal size. The pulse was rapid and regular, and the rate was 160 per minute (seated) at the first examination. The heart sounds were of normal quality and no murmurs were audible. The blood pressure was 120/80. No abdominal organs or masses were palpable. The extremities and central nervous system were normal.

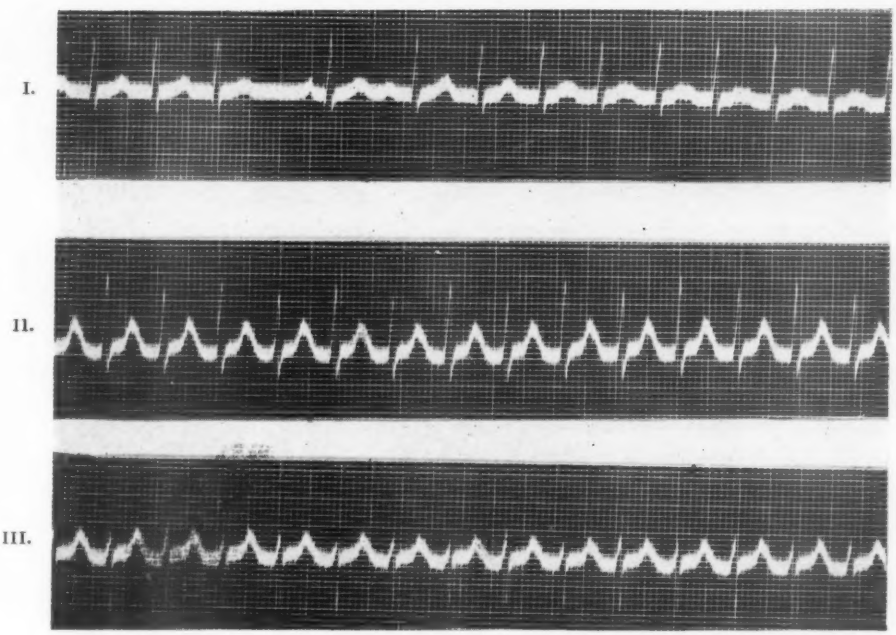

Fig. 6.—Case 2. Electrocardiograms taken Sept. 16, 1942, patient standing. Auricular tachycardia, rate 166 per minute. One sinus nodal beat in Lead I, with P-R interval of 0.12 second. P-R interval of first succeeding ectopic impulse, 0.16 second. Electrical alternation, R_2.

Laboratory Data.—The blood examination showed the following: hemoglobin, 12.5 Gm.; erythrocytes, 4,240,000; and leucocytes, 8,950, with a differential count of polymorphonuclear leucocytes, 57 per cent; lymphocytes, 30 per cent; monocytes, 3 per cent; and eosinophiles, 10 per cent. Slight anisocytosis was present. No abnormalities were detected on urinalysis. The blood sugar level was 85 mg. per 100 c.c., and the blood urea nitrogen was 15 mg. per 100 cubic centimeters. The blood Wassermann reaction was negative. The basal metabolic rate on two occasions was –16 per cent and –8 per cent, respectively. The Mantoux tuberculin reaction was negative with 0.1 c.c. of 1:100 O.T. A roentgenogram of the chest showed a normal cardiac silhouette and no abnormalities of the lungs.

Additional Cardiovascular Studies.—The patient was examined on forty-threee occasions over a period of three years. During this time she consistently showed a tachycardia which varied in rate with change in posture. The rate of the tachycardia in the different positions is discussed in the analysis of the electrocardiograms. On only one oc-

casion did digitalis therapy temporarily abolish the tachycardia. There was no response to quinidine or potassium salts. A tight abdominal binder had no influence on the pulse rate. The pulse rate was not influenced by exercise, respiration, or oculobulbar pressure. The tachycardia persisted during sleep. There was no appreciable or consistent response to carotid sinus pressure. On one occasion carotid sinus pressure was followed by a break in the tachycardia and two normal sinus beats before the paroxysm was resumed. On another occasion 2:1 A-V block was produced. Both of these effects may have been fortuitous. The blood pressure was normal and showed the normal range of postural variations.

Subsequent Course.—The patient moved to Florida at the end of 1943, and, unfortunately, we have been unable to follow her any further. During the period of observation her general health remained excellent, and she showed no symptoms or signs except her persistent tachycardia.

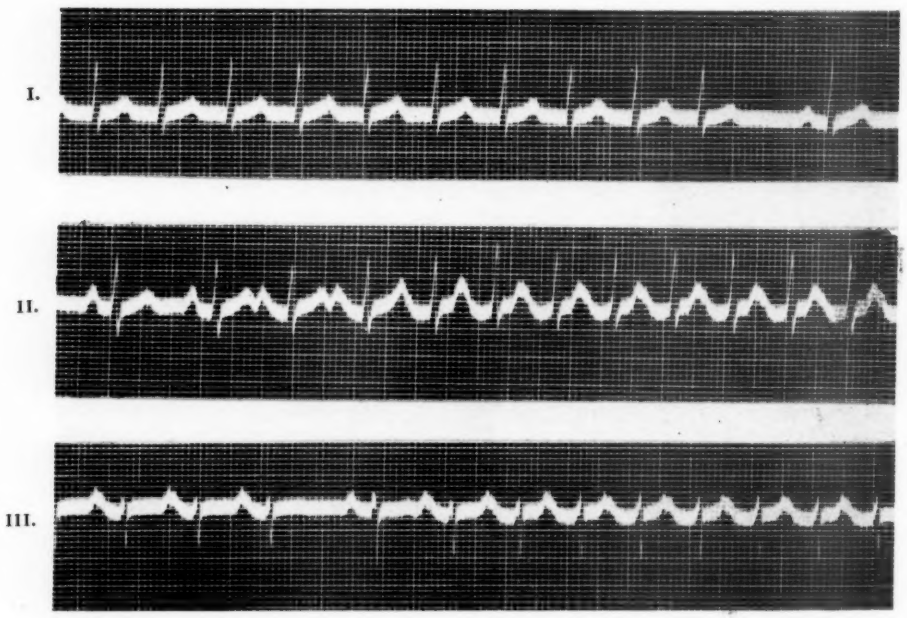

Fig. 7.—Immediately after Fig. 6, patient sitting. Rate of ectopic rhythm less, 158 per minute. One sinus nodal beat in Lead I, two in Lead II, and one in Lead III. P-R interval of normal sinus beats, 0.18 second. P-R interval of first ectopic beats, 0.22 second. Note gradual speeding up of rate of ectopic rhythm in Lead II.

Analysis of Electrocardiograms.—Electrocardiograms were obtained on thirteen occasions, in ten of which the influence of posture was investigated (Table I). There was invariably an auricular tachycardia which changed in rate with change of posture (Figs. 6, 7, and 8). The rate in the standing position ranged from 150 to 166 per minute; in the sitting position, from 125 to 158 per minute; and in the supine position, from 113 to 150 per minute. The maximum change in rate accompanying change from the vertical to the horizontal was 46 beats per minute, the minimum, 8 beats per minute. The change in rate was abrupt. Since in most instances the auricular complexes were superimposed upon the preceding ventricular deflections, the above rates are an approximation only. Accurate measurement of the auricular rate was also rendered impossible by the fact that the ventricular rate was inconstant because of varying A-V conduction. However, it was believed to be a fair assumption that, since the auricular rhythm was quite regular, the shortest R-R interval would closely approximate the true P-P interval, and the auricular rate was estimated accordingly.

The series of electrocardiograms shown in Figs. 6, 7, and 8 were especially selected from long strips to demonstrate the termination and onset of the tachycardia in the standing, sitting, and supine positions. In the illustrations several normal sinus beats are seen. The P-R interval corresponding to them was within normal limits, but varied with change of posture. There were very few normal auricular complexes throughout all of the electrocardiograms which were taken. In fact, only eighteen individual complexes of this nature were discovered out of a total of 2,312 auricular beats. On no occasion were more than two normal beats present in sequence. Two normal beats were found in the standing position, nine in the sitting, and seven in the supine. The runs of abnormal auricular beats ended in a postparoxysmal pause, and the first ectopic beat was premature. The aberrant P waves which gave rise to the tachycardia showed the following characteristics. In Lead I they

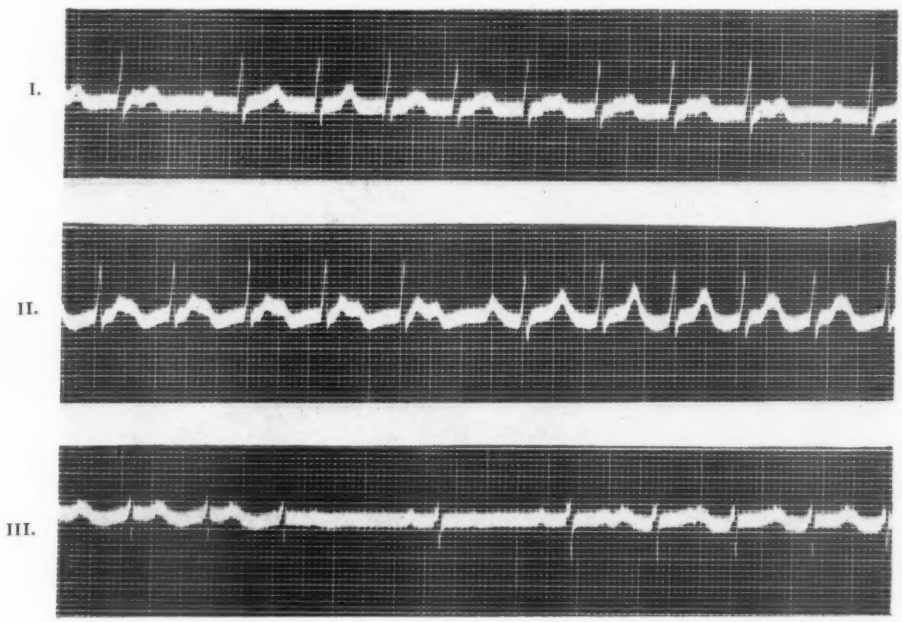

Fig. 8.—Immediately after Fig. 7. Patient supine. Further decrease in rate of auricular tachycardia, 130 per minute. Two normal sinus beats in Lead III, with P-R interval of 0.20 second. P-R interval of first ectopic beat, 0.24 second. (Note P-R interval of both normal and ectopic beats longer in recumbency than in sitting or standing positions.) Incomplete A-V block, with Wenckebach phenomenon during tachycardia.

TABLE I

ANALYSIS OF ELECTROCARDIOGRAMS IN CASE 2 WITH RESPECT TO RATE, PRESENCE OF DROPPED BEATS, AND NUMBER OF NORMAL SINUS BEATS IN THE STANDARD POSITIONS

DATE	AURICULAR RATE			DROPPED BEATS			NORMAL SINUS BEATS		
	STANDING	SITTING	SUPINE	STANDING	SITTING	SUPINE	STANDING	SITTING	SUPINE
11/15/40	158	150	125	–	–	–	1	0	0
12/14/40	166	158	133	–	–	+	0	1	0
2/13/41		125			+			1	
3/26/41	150	125	113	+	+	+	0	0	0
8/27/41	150	136	117	–	–	–	0	0	0
5/ 7/42	154	150	122	–	–	–	0	0	0
6/18/42		120			+			3	
7/ 8/42	158	150	117	–	–	–	0	0	0
7/23/42		150			–			0	
8/ 3/42	166	150	120	–	–	–	0	0	0
9/16/42	166	158	130	–	–	+	1	4	2
9/23/42	158	150	150	–	–	+	0	0	5
9/30/42	160	136	130	–	+	+	0	0	0

were of lower voltage than the normal P waves, whereas, in Leads II and III, they were taller and broader. They were followed by a well-marked auricular T wave, which caused a distinct sagging of the auricular S-T segment. The P-R interval corresponding to these abnormal

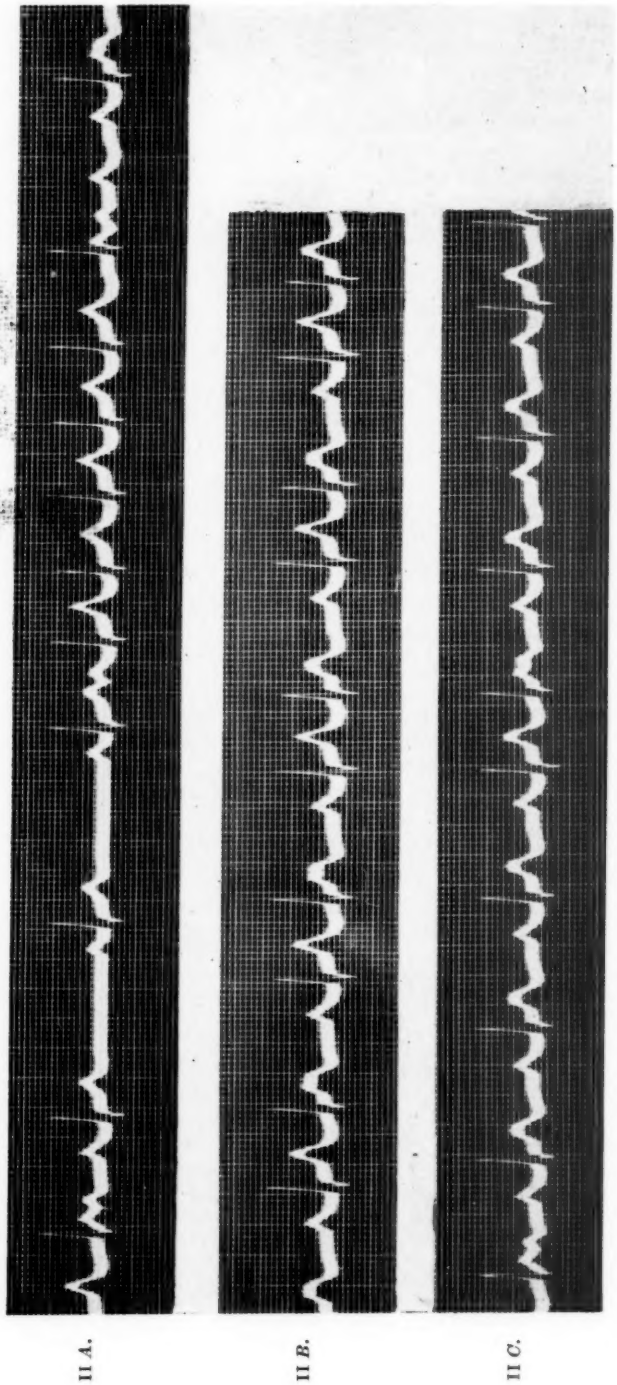

Fig. 9.—Sept. 23, 1942. Lead II, supine position. *A*, Note termination and onset of auricular tachycardia. P-R interval of first beat of tachycardia about 0.24 second. Well-marked auricular T wave after ectopic auricular beats. Progressive increase in P-R interval with, finally, two successive beats dropping out. P-R interval of next conducted beat about 0.26 second. *B*, Auricular tachycardia, 3:2 A-V block. *C*, Auricular tachycardia, 2:1 A-V block.

complexes was prolonged, and exceeded 0.20 second. This delay in the P-R interval was interpreted as indicating that an abnormal pathway had been taken by the wave of excitation in passing from the ectopic focus to the A-V node, rather than prolonged A-V conduction, because, even

when two ventricular beats dropped out (Fig. 9, *A*), the P-R interval of the first succeeding conducted beat was still lengthened. If the P-R delay were due to relative refractivity of the junctional tissues, recovery should have been expected after the rest period during the dropped beats. These abnormal auricular complexes were believed to be of ectopic origin for the following reasons: (1) distinctly aberrant appearance, (2) higher voltage than the normal sinus beats in Leads II and III, and (3) increased P-R interval. If these beats were of sinus nodal origin, with the pacemaker shifting to the lower portions of the node, the P waves should have been lower in voltage in Leads II and III, and the P-R interval, if altered, should have been shorter. It may be concluded, then, that the tachycardia was heterotopic in origin, and that its center was situated in the cranial portion of the right auricle. The ventricular complexes during the tachycardia were identical with those of the normal beats. Occasionally short periods of alternation of the QRS complexes were noted (Fig. 6).

Frequently, dropped beats, with or without Wenckebach periods, were present. At times only occasional beats dropped out, but at other times there was 3:2 or 2:1 block (Fig. 9, *B* and *C*). Incomplete A-V block was encountered only once in the standing position, four times in the sitting, and five times in the supine position. This phenomenon, in contrast to the prolongation of the P-R interval, is a definite indication of disturbed A-V conduction, functional in nature. It is probably the result of a combination of two factors, namely, fatigue, due to rapidity of the rate, and increased vagal tone, which accounts for its greater frequency during recumbency. On several occasions electrocardiograms were taken with the head of the table depressed at an angle of 30 degrees. This caused the auricular rate to be retarded below that in the supine position and increased the tendency to dropped beats.

Comment on Case 2.—This case was strikingly similar in most respects to the first one. In fact, the presence of a tachycardia which changed in rate upon change of position, without responding to the other sinus reactions, and with dropped beats in the supine position, led us to suspect its true nature clinically before securing electrocardiographic confirmation. Apparently this patient experienced no disability as a result of her tachycardia.

DISCUSSION

The arrhythmia which was present in these two cases was characterized by the following features: (1) chronicity. The tachycardia was invariably present when the patient was in the standing or sitting positions, and most often in the supine position, as well. (2) The arrhythmia originated in an ectopic auricular focus, in one instance in the left auricle, and, in the other, in the cranial portion of the right auricle. The tachycardia varied remarkably with change in posture. (4) The arrhythmia could not be terminated by carotid sinus stimulation. (5) Digitalis and quinidine therapy restored normal rhythm in Case 1. In Case 2 digitalis restored normal rhythm on only one occasion and quinidine was without effect. (6) Incomplete A-V block occurred in both cases, most commonly in the supine position. (7) Electrical alternation was observed in both cases.

These two cases are so bizarre that doubt must arise as to whether they actually fall into the category of paroxysmal auricular tachycardia. Case 1 has been cited twice since its publication, by Barker, et al.,[4] and Decherd, et al.[5] Both of these groups accepted it as an example of paroxysmal auricular tachycardia with incomplete A-V block. These

cases satisfied the following criteria for the diagnosis of paroxysmal auricular tachycardia: (1) The onset and termination of the tachycardia were abrupt. (2) It ended with a postparoxysmal pause. (3) The first auricular beat was premature. (4) The P waves were anomalous. (5) The rhythm in a given posture was fairly constant. (6) With certain exceptions, the arrhythmia did not exhibit the sinus reactions.

The possibility of a nomotopic rhythm may be excluded by the form of the auricular complexes. In Case 1 the P wave was inverted in Lead I and upright in Leads II and III, which suggested a locus in the left auricle.[2] In Case 2 the ectopic waves were higher than normal in Leads II and III, and consequently probably arose in the cranial portion of the right auricle. The absence of a consistent response to the sinus reactions in both cases and the response to digitalis and quinidine therapy in Case 1 also point to an ectopic origin of the tachycardia.

The tachycardia differed from typical paroxysmal auricular tachycardia in two important respects. First, since it occurred invariably as an orthostatic phenomenon and most of the time in the recumbent position as well, it was, in effect, the dominant and usual rhythm of these two hearts, or, in other words, it was a chronic arrhythmia. In this connection we may make mention of the fact that paroxysmal auricular tachycardia in many ways seems to be related closely to auricular flutter and fibrillation, and is possibly due to the same mechanism. Both of the latter may occur in either a paroxysmal or chronic form. Second, it did show some response to the sinus reactions. The rate of the tachycardia varied markedly with change in posture. Rarely, in Case 1, it showed some response to exercise. Carotid sinus stimulation, however, was without effect upon the auricular arrhythmia.

Little of fundamental importance has been added to our knowledge of the mechanism of paroxysmal auricular tachycardia since Lewis[6] reviewed the subject in 1925. Two main theories have been advanced in explanation of this arrhythmia, namely, (1) the theory of re-entry, of which circus movement is a variant, and (2) the theory of parasystole.

The theory of re-entry must be considered untenable unless the main objection, the presence of an isoelectric interval, be disposed of, as emphasized by Lewis.[6] Ashman and Hull,[7] and, more recently, Barker, et al.,[4, 8] attempted to dispose of this objection by suggesting either that the circus movement might involve in part of its pathway one of the auricular nodes, or that some part of the pathway might be so small that its action potential would not register in the electrocardiogram. We have been unable to reconcile the observations in our cases with this concept for the following reasons: (1) In our Case 1, as well as in several other reported cases of auricular tachycardia, the P wave was inverted in Lead I and upright in Leads II and III, presumably indicating that the impulse originated in the left auricle. If the circus pathway involved one of the nodes, the inscription of the auricular complex would begin at the moment the impulse made its exit from the node, and it is not conceivable that the foregoing P-wave pattern could result. As a possible rebuttal to this point, Ashman and Hull[7] called attention to an interesting observation by Glomset and Glomset,[9] namely, that tissue arrangement similar to that found in the region of the sinoauricular

node occurs in the left auricle around the mouths of the pulmonary veins, and suggested that possibly a circus movement could be set up in this region. (2) The rate of the tachycardia in the supine position was comparatively slow. On one occasion it was approximately 100 per minute (Fig. 5), with a corresponding P-P interval of 0.60 second. Since the auricular complex was 0.08 second in duration, the auricular isoelectric interval measured 0.52 second. It is hardly possible that the impulse would be delayed to such an extent in traversing the nodal tissues. (3) The change in rate on change of posture was too extreme to be explained reasonably on the ground of alteration of conductivity through the nodes or circus pathway. (4) An interesting phenomenon has been pointed out in Fig. 3. There was a break in the auricular tachycardia, and, after the postparoxysmal pause, the ectopic pacemaker resumed command of the heart. The first beat of the latter sequence could not be due to re-entry of the previous beat, but must be accepted as an impulse of spontaneous origin. This is an irrefutable argument against the possibility of re-entry in this particular case.

We believe that the theory of parasystole may be more applicable to our cases. The only convincing evidence for parasystole obtains in those rare instances in which the interval between ectopic beats is an exact, or nearly exact, multiple of a least common denominator, and when the ectopic beats appear at intervals which bear no fixed relationship to the normal sinus rhythm. These rigid criteria were not met in our cases. If, however, it be assumed that the rate of a parasystolic center might vary markedly in response to extracardiac influences, practically all cases of premature beats or paroxysmal tachycardia could be explained, although the proof of existence of parasystole would, in the process of accepting such an assumption, become all the more elusive.

The explanation of the arrhythmia in our cases, then, may be somewhat as follows: A parasystolic auricular focus was in continuous activity. There was a low degree of exit block, and, therefore, the parasystolic rhythm was the dominant one most of the time, and invariably in the upright position. It must be further assumed that the ectopic focus was under partial control of the extrinsic cardiac nerves, and responded in some degree to variations in vagal tone. The onset of the tachycardia in the upright position was thought to be due to a diminution in the tone of the vagus. Slowing of the rate in the sitting position was assumed to be due to reflexes from the lower extremities. Further retardation of the pulse or termination of the tachycardia in the recumbent or head-down position would coincide with additional vagal stimulation, either directly or reflexly through the carotid sinus by the sudden rush of blood to the head.[10]

The occurrence of incomplete A-V block in the two cases is of particular interest. In the first case it was found almost exclusively in the horizontal position, and, in the second, most frequently in this position. Clinostatic A-V block has been reported rarely, and has been explained as a postural vagal effect.[11, 12] Block occurred in the first case in the recumbent position only when the rate was relatively rapid. Therefore, the block resulted from a combination of two factors: fatigue due to rapid rate, and enhanced vagal tonicity. In Case 2 the P-R interval of both the normal sinus beats and the ectopic beats increased pro-

gressively as the patient changed position from the standing to the sitting, and from the sitting to the supine.

Electrical alternation was noted in both cases when the rate was excessively rapid.

The fact that we have had the experience of observing concurrently two bizarre cases of such striking similarity may have been a mere coincidence. However, it is quite possible that other cases of this nature may be overlooked and clinically may be mistaken for simple sinus tachycardia. If the electrocardiogram is recorded in one position only, and, as is common practice, in the recumbent position, normal sinus rhythm might be present, or, if the tachycardia should be in progress, the ectopic P waves may appear to be normal unless they happen to be markedly aberrant. If it were routine to take electrocardiograms in the three positions, standing, sitting and supine, in all atypical tachycardias, we believe more cases of this nature would be brought to light.

SUMMARY AND CONCLUSIONS

1. Two unusual cases of auricular tachycardia are presented. They fulfilled the electrocardiographic criteria for the diagnosis of paroxysmal auricular tachycardia, but differed from the classical type in two important respects, namely, the arrhythmia was chronic and it varied with change in posture.

2. The tachycardia was invariably present in the standing and sitting positions, and was present more frequently than normal sinus rhythm in the recumbent posture.

3. The rate of the tachycardia varied markedly on change of position. It was most rapid in the vertical, and slowest in the recumbent, position. One patient showed an occasional response to exercise, and also, in this case, the tachycardia could be abolished by digitalis or quinidine therapy.

4. In neither case was there any consistent response to carotid sinus stimulation.

5. In both cases there were clinostatic incomplete A-V block and orthostatic electrical alternation.

6. This symptom complex should be suspected clinically whenever there is a persistent orthostatic tachycardia which changes rate markedly on change of position, which does not respond to the other sinus reactions, and which is characterized by sudden breaks in rhythm. Electrocardiographic studies in the various postures should be carried out in these cases.

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WOLFF-PARKINSON-WHITE SYNDROME

REPORT OF FIVE CASES

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THE electrocardiographic syndrome of a short P-R interval with a long QRS complex in patients who are subject to attacks of paroxysmal tachycardia was first described by Wilson,[1] in 1915. Isolated cases were then reported by Wedd[2] and Hamburger.[3] It was not until 1930 that Wolff, Parkinson, and White[4] focused attention upon this clinical entity by reporting a series of eleven cases. They emphasized the benign nature of the condition. Since then, there have been several case reports from different parts of the world. The largest group of cases (twenty-two) was reported by Hunter, Papp, and Parkinson,[5] in 1940. They stated that this syndrome constituted 5 per cent of their cases of bundle branch block, and was present in 5 per cent of their patients who were subject to paroxysmal tachycardia. They collected one hundred nine cases from the literature.

Recently, five cases have come to our attention, two with unusual features. Three of the cases were observed in the Army. The benign nature of the condition had not been recognized on previous examinations. The important factor in ascertaining whether these patients should be retained in the Army or returned to civilian life depends upon the frequency and disability produced by the attacks of tachycardia, and not on the bizarre appearance of the electrocardiogram. If the attacks of tachycardia are infrequent and of short duration, and stopped promptly by vagus stimulation or abolished by quinidine, these patients may perform useful service in the Army. The purpose of this paper is to report the cases that we have observed.

CASE REPORTS

CASE 1.—This patient was a 29-year-old white man. There was a strongly positive history of vascular disease in his family. His father, mother, and brother have hypertension. There was no past history of rheumatic fever, chorea, syphilis, or hypertension. He had had "spinal meningitis" at the age of 15 years, with an uneventful recovery. His chief complaint was of eight attacks of palpitation since February, 1940. Each attack lasted only a few minutes, and the onset of each was sudden. The attacks stopped promptly when he held his breath or applied stimulation to the carotid sinus. The patient, a physician, stated

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that he had had "left bundle branch block" in his electrocardiogram on several examinations since 1940. The current tracings appeared identical to previous electrocardiograms.

On examination, his blood pressure was 138/84. The peripheral arteries were normal. The fundi showed no evidence of retinal vascular disease. The heart size was normal. The heart rhythm was regular, and no murmurs were heard. An exercise tolerance test was normal. The sedimentation rate was 5 mm. (Westergren method). The blood and urine were normal. The blood nonprotein nitrogen was 31 mg., and the sugar, 99 mg., per cent. The blood Kahn reaction was negative. The heart size was normal on roentgenologic examination. An electrocardiogram (Fig. 1) showed the short P-R interval, of 0.10 to 0.12 second, and long QRS interval, of 0.16 second, which are characteristic of this condition. Atropine and exercise had no significant effect upon this electrocardiogram. Because the patient was a young physician, with infrequent attacks of paroxysmal tachycardia which were promptly controlled by carotid sinus stimulation, he was accepted for limited duty in the Army, confined to the continental United States.

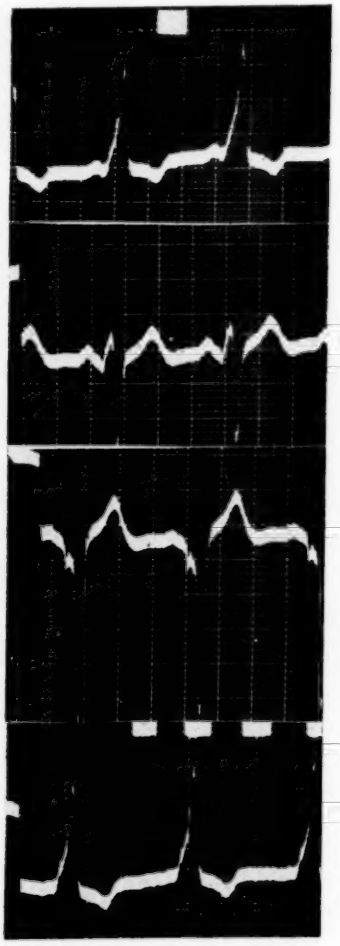


Fig. 1.—Case 1. Description in text.

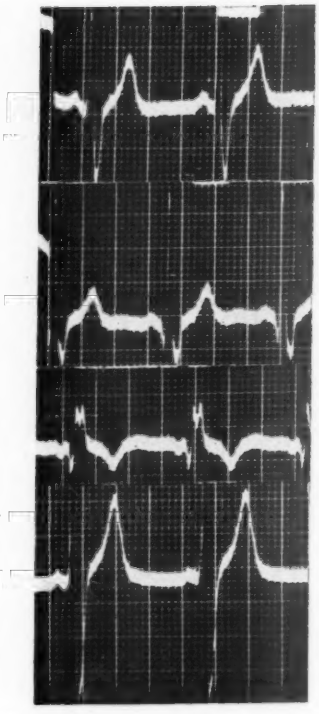
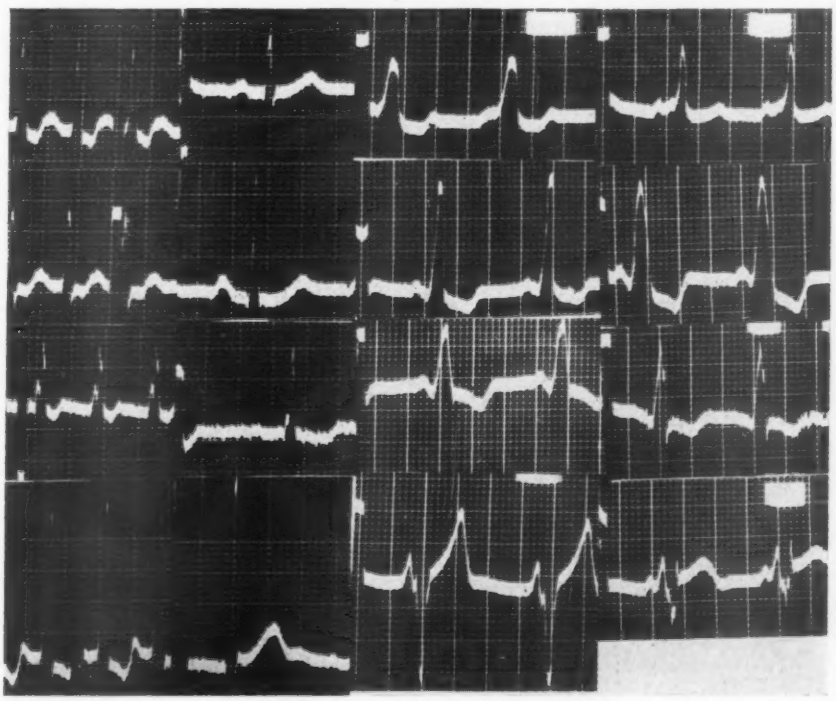


Fig. 2.—Case 2. Description in text.

CASE 2.—This patient was a 30-year-old white man, also a physician. There was a strongly positive history of vascular disease in his family. His father has angina pectoris and his mother has hypertension. The only significant previous illness was cystitis, in 1931, after a lower urinary tract operation for hypospadias. He had had slight elevation of his blood pressure on several examinations during the preceding seven years. The highest reading, to his knowledge, was 170/110. He stated that he had an electrocardiogram at the age of 23 years which showed "delayed interventricular conduction time." That tracing was not available to us, but he stated that it appeared similar to the present electrocardiogram.

On examination, his blood pressure was 150/110. The peripheral arteries were normal. The fundi showed no evidence of retinal vascular disease. The heart was normal size. The heart rhythm was regular and no murmurs were heard. The heart size was normal on roentgenologic examination. The blood and urine were normal. The blood nonprotein nitrogen was 35 mg. per cent, and the phenolsulfonphthalein excretion, 75 per cent. His urine concentrated to 1.024 and diluted to 1.002. The sedimentation rate was 4 mm. (Westergren method), and the blood Kahn reaction was negative. An excretion pyelogram was normal. An electrocardiogram (Fig. 2) showed a short P-R interval, of 0.10 to 0.12 second, and a long QRS interval, of 0.12 second. An unusual feature of this case was inversion of the P waves in Lead III. The P waves are supposedly upright in all leads in this syndrome. Subsequent tracings were identical with this one.

This patient was a physician. He did not have attacks of tachycardia, so that he was not disabled by this syndrome. He was reclassified on a limited duty status, confined to the continental United States because of the hypertension, and not because of his electrocardiogram.



a. *b.* *c.* *d.*

Fig. 3.—Case 3. Description in text.

Case 3.—This patient was a 29-year-old, white, male officer. There was no history of vascular disease in this patient's family. He had not had rheumatic fever, chorea, syphilis, or hypertension. His chief complaint was of recurrent attacks of palpitation during the preceding year. The attacks began suddenly, lasted several hours each time, and were relieved by lying down, bending over, or holding his breath.

On physical examination, his blood pressure was 110/68. The retinal vessels and peripheral arteries were normal. Examination of the heart was negative. The urine, blood, and Kahn reaction were negative. The sedimentation rate was 2 mm. (Westergren method). The blood nonprotein nitrogen was 31 mg., and the sugar, 78 mg., per cent. The heart size was normal on roentgenologic examination. An electrocardiogram (Fig. 3, *a*), taken Oct. 30, 1943, showed auricular tachycardia, with a rate of 180. Fig. 3, *b* shows a normal tracing, with a P-R interval of 0.20 second and a QRS interval of 0.08 second; this was recorded Dec. 7, 1943. Fig. 3, *c* shows the characteristic short P-R interval (0.09 second) and long QRS interval (0.14 second). Forty minutes after $\frac{1}{75}$ grain of atropine subcutaneously, the QRS interval was shortened slightly in Lead I (Fig. 3, *d*). Fig. 4

shows normal sinus rhythm, with extrasystoles characteristic of the Wolff-Parkinson-White type, occuring as bigeminy in Lead II. Fig. 5 shows a strip of Lead II. There are normal beats, ventricular extrasystoles, and extrasystoles similar to the Wolff-Parkinson-White beats leading to paroxysmal auricular tachycardia.

This patient's attacks of tachycardia were controlled by quinidine. He was not thought to be incapacitated by the infrequent attacks of tachycardia, which were controlled by quinidine. He was therefore reclassified to a limited duty status, confined to the continental United States.

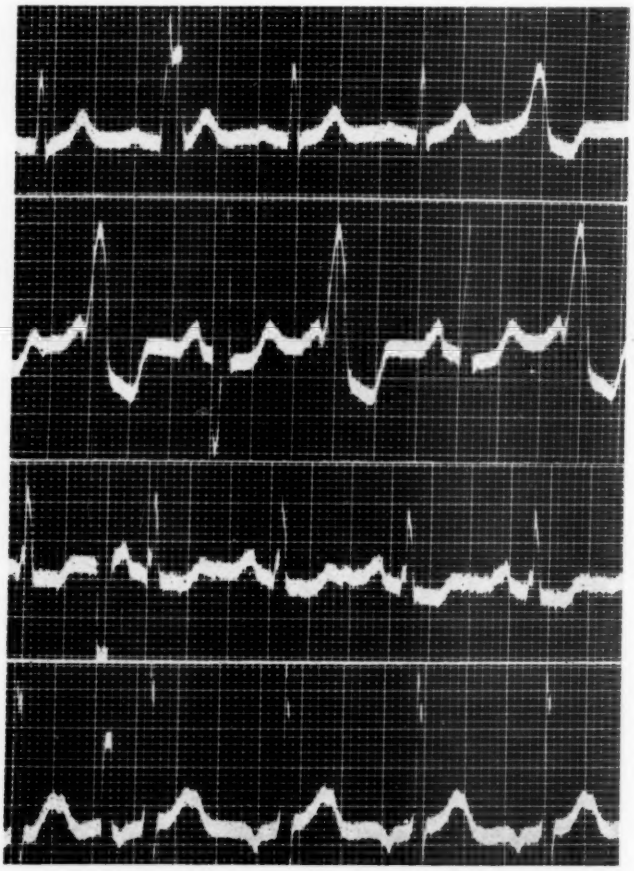


Fig. 4.—Case 3. Description in text.

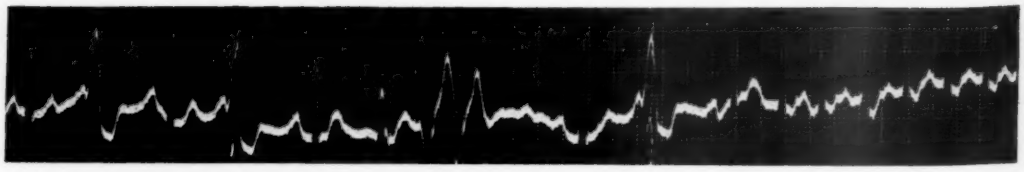
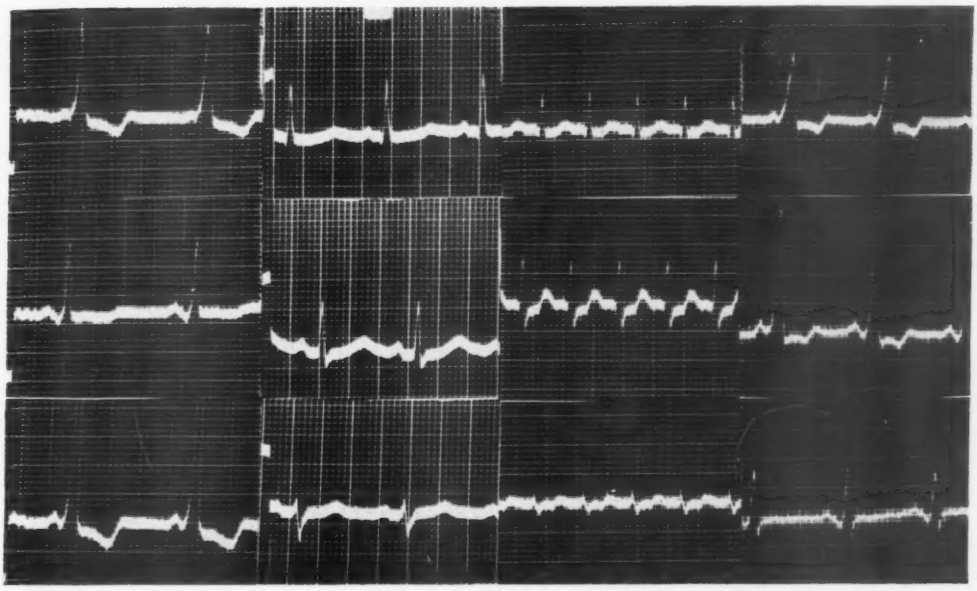


Fig. 5.—Case 3. Description in text.

CASE 4.—This patient was 26 years old when he first came under observation by one of us (R. W. R.) in October, 1939. There was no history of vascular disease in his family. He had not had rheumatic fever, syphilis, or hypertension. His chief complaint was of frequently recurring attacks of palpitation for five months. The attacks were usually short in duration, lasting only a few minutes, but recurred almost daily. There were no symptoms of heart failure or angina.

On physical examination, his blood pressure was 125/70. His heart was of normal size, the rhythm was regular, and no murmurs were heard. The retinal vessels and peripheral arteries were normal. The urine, blood, and Kahn reaction were negative. The sedimenta-



a. *b.* *c.* *d.*

Fig. 6.—Case 4. Description in text.

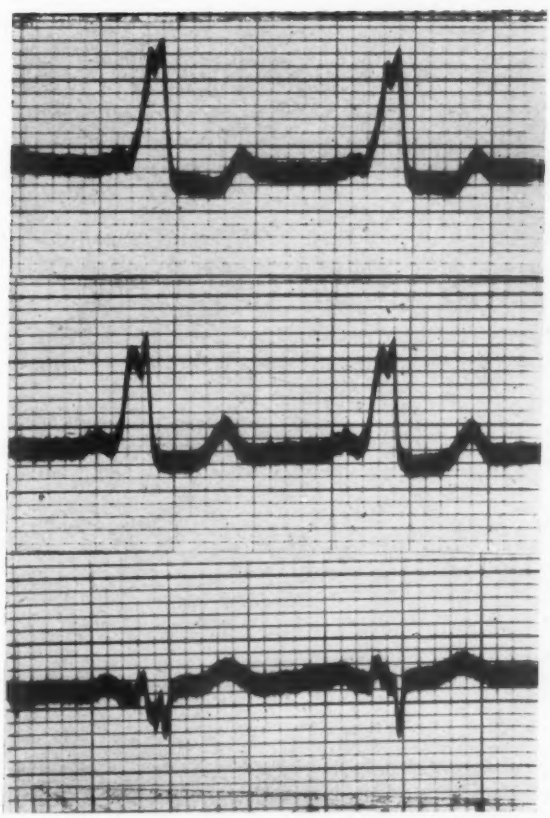


Fig. 7.—Case 5. Description in text.

tion rate was 4 mm. (Westergren method). The blood nonprotein nitrogen was 32 mg., and the sugar, 84 mg., per cent. The blood Kahn reaction was negative. The heart was of normal size on roentgenologic examination. An electrocardiogram (Fig. 6, *a*) taken Oct. 16, 1939, showed the characteristics of this syndrome, with a P-R interval of 0.10 second and a QRS interval of 0.12 second. Frequent tracings since then have been the same. However, a normal tracing was obtained Nov. 2, 1941 (Fig. 6, *b*), with a P-R interval of 0.18 second and a QRS interval of 0.08 second. On July 21, 1942, a supraventricular tachycardia, with a rate of 185, was recorded (Fig. 6, *c*). Another tracing, taken Sept. 2, 1942, still showed the electrocardiographic features of this syndrome (Fig. 6, *d*).

The patient had daily attacks of tachycardia, even when he was taking quinidine. He would therefore be unable to qualify as a soldier in the Army. He would in all probability be disqualified because of the disability produced by his attacks of tachycardia, and not because of the bizarre electrocardiogram.

CASE 5.*—This patient was an 18-year-old white girl. The past and family histories were negative. The patient had never had an attack of paroxysmal tachycardia or other symptoms referable to her heart. On Feb. 15, 1944, she had a sore throat. Two days later she experienced migrating joint pains, malaise, erythema nodosum, and fever.

On examination, her blood pressure was 116/68. The temperature was 102° F. The peripheral arteries were normal. The fundi showed no evidence of retinal vascular disease. The heart was of normal size. The heart rhythm was regular, and a soft systolic murmur was heard at the pulmonic area. The heart was of normal size on roentgenologic examination. The leucocyte count was 13,000, and the sedimentation rate, 84 mm. (Wintrobe method). The urine and the blood Kahn reaction were negative. An electrocardiogram (Fig. 7) showed the short P-R interval and long QRS interval characteristic of this condition. Subsequent tracings were identical with this one. The joint pains, fever, and erythema nodosum responded promptly to 20 grains of aspirin four times daily. There were no complications during her convalescence from rheumatic fever.

This was a case of rheumatic fever in a patient with the Wolff-Parkinson-White syndrome. The P-R interval did not become prolonged during the course of the rheumatic fever.

DISCUSSION

There were a few unusual features in these cases. It is characteristic for the P waves to be upright in the conventional leads. In Case 2, the P waves were diphasic or inverted. In Case 3 there was the unusual feature of normal beats, ventricular premature beats, and premature beats of the Wolff-Parkinson-White type leading into paroxysmal auricular tachycardia. In Case 3, also, normal beats alternated with premature beats which were identical with the beats of the Wolff-Parkinson-White type observed at other times in this patient, occurring as a bigeminy.

This syndrome is being recognized with increasing frequency. If there is no associated heart disease, the condition is apparently benign. If the patients are disabled by it, it is because of the associated attacks of paroxysmal tachycardia, and not the result of the bizarre electrocardiogram.

SUMMARY

Five cases of the Wolff-Parkinson-White syndrome have been presented, with comments upon some unusual features encountered. These patients may be able to perform useful service in the Army if they are not incapacitated by frequent attacks of paroxysmal tachycardia.

We wish to express our appreciation to Dr. S. A. Levine, of Boston, for his aid in interpreting some of the electrocardiograms. We are indebted to Colonel James S. Sweeney, Chief of the Medical Service at Bushnell General Hospital, for many helpful suggestions and the editing of this paper.

*We are indebted to Dr. J. C. Hayward of Logan, Utah, for permitting us to include this case in our series.

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THE PROGNOSTIC SIGNIFICANCE OF AURICULAR FIBRILLATION IN ASSOCIATION WITH MYOCARDIAL INFARCTION

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AURICULAR fibrillation is infrequently associated with myocardial infarction. Prognostically, it has not been regarded as a serious complication alone, but rather as a reflection of an advanced degree of cardiac failure. It has been regarded as usually transient, requiring no specific consideration. Because of its infrequency, no large series of cases has been analyzed. Master, Dack, and Jaffe[1] found 22 instances among 300 patients with myocardial infarction (7.3 per cent); Rosenbaum and Levine[2] found 25 among 208 patients (12 per cent), and Rathe,[3] 35 among 274 patients (12.7 per cent).

MATERIAL

We have studied 84 patients with auricular fibrillation; this occurred in a group of 1,247 patients with myocardial infarction who were admitted to the Los Angeles County General Hospital, an incidence of 7.7 per cent. This paper concerns itself only with the prognostic significance of the arrhythmia in these cases. The diagnosis of myocardial infarction was accepted only when the history and electrocardiogram were typical. Auricular fibrillation was diagnosed only when confirmed by electrocardiograms. Probably many cases of transient fibrillation, with no tracings, were overlooked. Therefore, the figures do not actually represent the incidence of the arrhythmia in its transient form. They should, however, represent the incidence of the persistent form in this group. Contrary to expectations, auricular fibrillation was found to be persistent in a large number of cases. In 29 instances the arrhythmia disappeared; in 55 it persisted.

MORTALITY RATES

The mortality among the 1,247 patients with myocardial infarction during their hospitalization (about one month) was 642, a rate of 51.5 per cent (Table I). The 84 patients with auricular fibrillation had a definitely higher death rate. In the 29 cases in which the arrhythmia disappeared, the mortality rate

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TABLE I. COMPARISON OF MORTALITY IN CASES IN WHICH AURICULAR FIBRILLATION DISAPPEARED AND IN THOSE IN WHICH IT PERSISTED

	MORTALITY (%)
1,247 (whole group)	51.5
84 (with auricular fibrillation)	79.8
29 (in which arrhythmia disappeared)	58.6
55 (in which arrhythmia persisted)	89.4

TABLE II. RELATION OF TIME OF DEVELOPMENT OF AURICULAR FIBRILLATION TO THE DISAPPEARANCE OR PERSISTENCE OF THE ARRHYTHMIA

RELATION TO TIME OF MYOCARDIAL INFARCTION	AURICULAR FIBRILLATION		MORTALITY
	DISAPPEARED	PERSISTED	
8 (preceded)	1	7	99.0
41 (coincident)	1	40	81.8
35 (followed)	27	8	72.0

was only slightly increased. In the 55 cases in which it persisted, the death rate was markedly increased. The persistence was apparently the most important factor about the arrhythmia which influenced mortality. Persistence of auricular fibrillation was found to be correlated both with the time of onset of the arrhythmia and with the degree of pre-existing cardiac damage (Table II). In nearly all cases in which the auricular fibrillation preceded or coincided with the onset of the myocardial infarction, the arrhythmia persisted, whereas, in nearly three-fourths of those in which the auricular fibrillation occurred after myocardial infarction, the arrhythmia disappeared.

COMPARISON OF PERSISTENT GROUP WITH TRANSIENT GROUP (TABLE III)

The group with persistent auricular fibrillation showed evidence of marked pre-existing cardiac damage. In this group, as contrasted with the group in which the arrhythmia disappeared, twice as many gave histories of signs and symptoms of previous cardiovascular disease, such as hypertension, dyspnea, and edema (83.6 per cent as compared with 41.3 per cent). One-half gave histories or had necropsy evidence of previous infarcts, and nearly three-fourths had congestive failure. A surprising discovery was the number who died with clinically suspected systemic emboli. Nearly one-third of the deaths in the group with persistent auricular fibrillation were due to such emboli, as contrasted to only one-ninth in the group in which the arrhythmia disappeared. The conversion to sinus rhythm was not as productive of emboli as was the persistence of the arrhythmia.

Clinically suspected embolism in the greater circulation, only, was considered. Pulmonary embolism may often arise from peripheral venous thrombi, but sudden hemiplegia or sudden arterial obstruction in an extremity, if due to embolism, can arise only from the left side of the heart, save in paradoxical embolism due to anomalies of the cardiac septa.

TABLE III. COMPARISON OF PERSISTENT GROUP WITH TRANSIENT GROUP

AURICULAR FIBRILLATION	AVERAGE AGE (YRS.)	PREVIOUS CARDIOVASCULAR DISEASE	PREVIOUS INFARCTS	CONGESTIVE FAILURE	SYSTEMIC EMBOLI	DEATHS
Transient (29)	66	12 (41.3%)	2 (6.9%)	7 (24%)	2 (11%) (of deaths)	17 (58.6%)
Persistent (55)	68	46 (83.6%)	30 (52.6%)	41 (71.8%)	15 (29.4%) (of deaths)	51 (89.4%)

Persistent auricular fibrillation, therefore, produced a very high death rate (89.4 per cent). In 85 per cent, the arrhythmia appeared in the first electrocardiogram and was usually associated with congestive failure. One-third of the deaths were due to systemic arterial emboli.

THE EFFECT OF MEDICATION

Although auricular fibrillation tended to disappear in the majority of patients who received quinidine alone, and to persist in the majority of patients who received digitalis alone (Table IV), the effect of the medication was not conclusive. Quinidine alone was used for patients with little pre-existing heart damage, in many of whom the arrhythmia was recent and might spontaneously have disappeared, whereas digitalis alone was used for those with marked pre-existing damage, in many of whom the arrhythmia was already established. Digitalis is not used to terminate auricular fibrillation, whereas quinidine is. It is impossible to predict, therefore, whether or not the auricular fibrillation would have disappeared anyway in those cases in which quinidine apparently stopped the arrhythmia. It is also impossible to predict what the effect upon the arrhythmia would have been had quinidine been given in addition to digitalis in those cases in which the auricular fibrillation persisted.

TABLE IV. RELATION OF TYPE OF MEDICATION TO THE DISAPPEARANCE OR PERSISTENCE OF AURICULAR FIBRILLATION

MEDICATION	NUMBER	NUMBER DISAPPEARED	NUMBER PERSISTED
None	17	5	12
Quinidine alone	11	9	2
Digitalis alone	44	6	38
Digitalis and quinidine	12	9	3
Total	84	29	55

THE EFFECT OF PRE-EXISTING CARDIAC DAMAGE

Since marked pre-existing cardiac damage was so closely correlated with persistent auricular fibrillation, one must ask whether the damage alone was responsible for the high mortality and the high incidence of embolism. Can one ignore the arrhythmia, per se, in the prognosis, and predict the outcome upon the basis of the cardiac damage alone? If so, patients with myocardial infarction and congestive failure, but with no auricular fibrillation, should show approximately the same mortality rate and incidence of embolism as a similar group in which auricular fibrillation was the only other complication (Table V).

The incidence of embolism was much lower, however, when no auricular fibrillation occurred (7 per cent as compared with 34 per cent), indicating that the arrhythmia increased the hazard of embolism. This was further suggested

TABLE V. MORTALITY AND CLINICALLY RECOGNIZED EMBOLISM (SYSTEMIC) IN MYOCARDIAL INFARCTION

(Effect of Congestive Failure and Auricular Fibrillation)

PATIENTS WITH MYOCARDIAL INFARCTION	MORTALITY (%)		PERCENTAGE OF SYSTEMIC EMBOLI		NUMBER OF CASES	
	WITHOUT AURICULAR FIBRILLATION	WITH AURICULAR FIBRILLATION	WITHOUT AURICULAR FIBRILLATION	WITH AURICULAR FIBRILLATION	WITHOUT AURICULAR FIBRILLATION	WITH AURICULAR FIBRILLATION
With congestive failure	83.0	89	7	34	85	48
No congestive failure—no previous infarcts	43.4	66	4	16	76	36

by the effect of auricular fibrillation complicating myocardial infarction in the absence of congestive failure. Of two groups with myocardial infarction, but no congestive failure and no known previous infarcts, in which the presence of auricular fibrillation in one group was the only variable, both the mortality rate and the incidence of systemic emboli were markedly increased in the one in which the arrhythmia was present. Persistent auricular fibrillation, therefore, was a hazard whether it was imposed upon previously damaged hearts or upon previously undamaged hearts.

SUMMARY OF OBSERVATIONS

1. The mortality rate among patients with myocardial infarction plus auricular fibrillation was much higher than in a group without auricular fibrillation.

2. Prognostically, if the auricular fibrillation disappeared in one day, the mortality rate was slightly increased; if it persisted longer than one day, the mortality rate increased markedly.

3. If no reversion to sinus rhythm occurred, death ensued in 89 per cent. One-third of the deaths were due to clinically recognized systemic emboli.

4. Persistence of the arrhythmia could be correlated with pre-existing cardiac damage.

5. Cardiac damage, however, was not the sole cause of the high mortality rate and high incidence of embolism.

6. Auricular fibrillation increased the mortality rate and incidence of embolism, regardless of whether congestive failure was or was not present.

7. Whether or not auricular fibrillation was found in the first electrocardiogram was a fairly reliable way of predicting whether the arrhythmia would be persistent or transient. In only eight of the 55 cases in which auricular fibrillation was found in the first tracing did the arrhythmia disappear, whereas, in 27 of 35 in which the arrhythmia followed myocardial infarction, sinus rhythm returned. If the auricular fibrillation definitely followed myocardial infarction, the prognosis was about average if it disappeared in one day or less; but if it lasted over one day, the prognosis was much worse because then the arrhythmia persisted in about one-third. The worst prognosis was among those whose auricular fibrillation was known to have existed before (99 per cent mortality, with 57 per cent dying of systemic embolism), and among those who had had a previous infarct (96 per cent mortality, with 30 per cent systemic embolism). Only congestive heart failure with enlargement of the liver and edema of the ankles was considered.

RELATION TO LOCATION OF INFARCT

There was no correlation of the auricular fibrillation with the location of the infarct. Wood, Wolferth, and Bellet[4] found a high incidence of auricular fibrillation in association with lateral infarction of the left ventricle. Thomson

TABLE VI. LOCATION OF INFARCTS AT NECROPSY IN FIFTY-ONE CASES OF MYOCARDIAL INFARCTION AND AURICULAR FIBRILLATION

	NO.	%
Left lateral wall (recent)	8	16
Left lateral wall (old) plus posterior infarction (recent)	3	6
Interventricular septum	3	6
Anterior and posterior (combined)	2	4
Posterior	14	28
Anterior	21	42

and Feil[5] recently published a similar report. In fifty-one of our patients with auricular fibrillation, necropsy revealed no significantly higher incidence of lateral wall infarctions than is found in a group without auricular fibrillation. The percentage distribution of the location of the infarction was much the same as in patients with no auricular fibrillation (Table VI).

CAUSE OF AURICULAR FIBRILLATION

What causes auricular fibrillation to appear in association with myocardial infarction? Auricular anoxemia and vagal stimulation are apparently the important factors in its production in the experimental animal.[6] Congestive failure and auricular distention are apparently important to the extent that they induce auricular anoxemia, but neither is essential for the production of auricular fibrillation. Vagus stimulation alone has produced auricular fibrillation in the dog.[7] Apparently, in coronary artery insufficiency, there is hypersensitivity to vagal stimuli, as suggested by the increased sensitivity of the carotid sinus reflex.[8] The production of auricular fibrillation would seem to be determined by the degree of vagal activity, the degree of auricular anoxemia, and the individual susceptibility of the patient. A higher percentage should therefore be found among the patients with congestive failure, and the auricular fibrillation should persist longer. This was found to be true. Although it was impossible in most instances to ascertain which was the precursor, congestive failure or auricular fibrillation, they were associated in forty-eight instances. In these cases the arrhythmia usually persisted. Congestive failure was not necessary to precipitate the arrhythmia, however. Auricular fibrillation occurred in thirty-six cases without congestive failure. In most of these the arrhythmia disappeared.

DISCUSSION

This series was surprising because of the large number whose auricular fibrillation persisted until death. Forty-seven of the fifty-five patients with persistent auricular fibrillation showed the arrhythmia in the first tracing, so that it was impossible to know in how many it existed before the onset of myocardial infarction. Levine[9] believes that myocardial infarction occurs rarely in patients with persistent auricular fibrillation, but in eight of our cases the arrhythmia had been demonstrated in previous tracings and out-patient examinations. In how many of the others it existed prior to the onset of infarction is unknown.

It is apparent that severe, long-standing cardiac damage was the cause of persistent auricular fibrillation. Despite the severity of the underlying damage, however, the data would suggest that the arrhythmia was definitely an additional hazard, increasing the death rate in general, and systemic embolism, in particular, over and above that which would result from the cardiac damage alone.

The concept that auricular fibrillation is not a significant prognostic hazard when associated with myocardial infarction has been based upon the premise that it is transitory, and that it is the associated shock and heart failure, rather than the arrhythmia, which is dangerous. The above series demonstrates that auricular fibrillation may not be a serious prognostic factor if it is transitory, but that the persistent form is not necessarily uncommon, and constitutes a definite prognostic hazard. The elimination of an ectopic rhythm which increases the load upon a badly damaged heart by increasing

ventricular rate and by increasing the possibility of fatal systemic emboli would seem imperative. The factors to be considered are complex, and will be dealt with in another study.

CONCLUSIONS

Auricular fibrillation in association with myocardial infarction in a series of eighty-four patients at the Los Angeles County General Hospital was a hazard as regards both mortality rate and the incidence of systemic emboli.

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GASTROINTESTINAL SYMPTOMS OF PROGRESSIVE MYOCARDIAL DISEASE

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STATEMENTS can be found in medical literature to the effect that gastrointestinal symptoms are of common occurrence in primary heart disease, and that these symptoms may largely overshadow the more typical symptoms of heart failure. Thus, in 1892, Osler[1] made the observation that "cases of cardiac insufficiency which do badly and fail to respond to digitalis are most often those in which nausea and vomiting are prominent symptoms." Likewise, Herrick,[2] in his original article on the clinical features of coronary occlusion, remarked that "nausea and vomiting with belching of gas are quite common." Prior to the publication of Herrick's classic paper, and indeed even up to the present writing, the acute phase of coronary occlusion has often received the misnomer of "acute indigestion."

In spite of these and other isolated instances, it is rather remarkable that so little attention has been directed to the gastrointestinal symptoms of congestive heart failure from the point of view of diagnosis, prognosis, or treatment, and the rather meager experimental work in this field has not been given

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full clinical application or led to more illuminating studies. It is, therefore, our purpose to review briefly the literature on nausea and vomiting as manifestations of severe cardiac disease, outlining some current concepts of the underlying pathologic physiology, and to present a case of progressive myocardial failure in which gastrointestinal symptoms dominated the clinical picture and resisted all therapy; their steadily increasing severity paralleled the fatal course of events.

Levine[3] states that there are many instances of congestive heart failure in which nausea, abdominal distress, and often vomiting occur. Harrison[4] reports that occasionally these symptoms occur in patients with chronic congestive failure and in myocardial infarction; in the former they are ascribed to venous congestion of the liver and stomach. Christian[5] and Tice[6] also make brief references to the occurrence of nausea and vomiting in heart disease. The fact that these various authors recognize that these symptoms are at least occasionally a part of the clinical picture of chronic heart failure leads one to conclude that their occurrence is not uncommon, although no statistical data are available to support this belief.

That the presence of nausea and vomiting does not necessarily imply a primary disturbance of the digestive tract is all too frequently lost sight of by the physician, and perhaps accounts for the relative scarcity of clinical correlation between primary cardiac disease and gastrointestinal symptomatology. The common fallacy of ascribing these symptoms directly to the digestive tract is evident when one recalls the pharmacologic action of such drugs as digitalis and apomorphine. Hatcher and Weiss[7] showed experimentally that the emetic effect of digitalis bodies was exerted by reflex action directly from the heart itself. They further concluded that the heart proper is frequently the seat of the vomiting reflex induced by primary disease of this organ.[8, 9] This concept is supported by the work of Sutton and King,[10] who found that, in conscious dogs, traction upon a ligature passed loosely about a coronary artery and brought out through the thoracic wall was followed by vomiting and apparent nausea. It was further demonstrated by these two groups of authors, who were working independently, that the afferent arc of this reflex is chiefly by way of the sympathetics, and, in part, probably by the vagi to the vomiting center in the region of the sensory nuclei of the vagi near the floor of the fourth ventricle. The efferent pathways of the reflex of nausea and vomiting are well understood and will not be discussed here. Further interrelationships of the heart and stomach have been noted by Manning, Hall, and Banting,[11] who found marked congestion, with hemorrhages, in the stomach and duodenum, along with infarctions of the myocardium, after repeated stimulation of the vagus nerve in dogs. Gilbert, Fenn, and LeRoy[12] produced reflex coronary vasoconstriction in dogs by initiating vagal stimulation in the gastrointestinal tract. Likewise, Levy and Boas[13] showed that patients with peptic ulcer who later developed angina pectoris had their angina in the form of epigastric pain, often simulating the pain of peptic ulcer as experienced previously, but with the typical causal factors of exertion and emotion.

The studies discussed above may be summarized as follows: (a) Disorders of the heart may produce reflex disturbances of the stomach, and vice versa. (b) Nausea and vomiting are not uncommon symptoms of cardiac disease, especially disease resulting from inadequate coronary flow. (c) These symptoms may, under certain conditions at least, be induced reflexly from the heart itself. The following case seems to illustrate these several points.

CASE REPORT

A. R., a 44-year-old white merchant, was admitted to the private medical service of the North Carolina Baptist Hospital with an illness of about two months' duration. He had been known to have hypertension for approximately ten years, and his family physician had found his blood pressure as high as 240/140 on frequent occasions. He had, however, been active and relatively free of symptoms until his present illness. He had complained of slight dyspnea and of "twinges of pain in the chest" on exertion for several years, but these were never severe, required no medication, and produced no disability.

On Jan. 28, 1943, two months prior to admission, the patient awakened early in the morning with a feeling of nausea which became progressively more severe. This was accompanied by a sense of substernal oppression, and he vomited several times. He complained chiefly of the nausea and vomiting, but was moderately dyspneic and stated that his physician noted a fall in his blood pressure.

The diagnosis of coronary occlusion was determined upon, and the patient remained in bed for the next three weeks, after which he gradually resumed his work in his store. During his convalescence he continued to complain of severe nausea which was relieved only by vomiting. These symptoms occurred as often as three to five times a day; the vomitus was yellowish green, without blood. He was receiving no digitalis at this time.

He showed gradual improvement and returned to work, but three weeks prior to admission he was again awakened during the night by severe nausea, vomiting, and a sensation of constriction in his chest. He was taken to another hospital, where he remained until being transferred to the Baptist Hospital. In the interim he had been given digitalis and aminophylline without improvement. Tachycardia at a rate of 140 per minute was noted. This persisted and resisted the above therapy, as did the nausea and vomiting.

The family history revealed that one brother had died of hypertension, one brother had hypertension and was living, and one son, aged 20 years, had been rejected by the Army Medical Corps because of high blood pressure.

Physical Examination.—On March 30, 1943, the date of admission, the patient's temperature was 36.8 C. (98 F.), his pulse rate, 140 per minute, and his respirations, 28 per minute. The systolic blood pressure was 158 mm. Hg, and the diastolic pressure was 148, with complete disappearance of sounds at 135 mm. Hg, resulting in a pulse pressure of only 10 mm. of mercury.

The patient was a heavy-set, ruddy-faced male, appearing chronically ill. His breathing was of the Cheyne-Stokes variety, and the neck veins were moderately distended. Ophthalmoscopic examination revealed marked narrowing of the arterioles, with advanced arteriovenous nicking and mild papilledema. There was no hemorrhage or exudation. The chest was symmetrical, with fair expansion; there were diminished breath sounds in both bases, and also a few scattered, moist, crackling râles. The cardiac dullness was remarkably increased and extended to the anterior axillary line in the fifth left intercostal space. The entire precordium appeared to shiver during systole, and the apex impulse was not well localized. The sounds were clear and of moderate intensity, and a presystolic gallop rhythm was heard, best at the apex. The radial pulses were of small volume, equal, and regular.

The abdomen was pendulous and showed no spasm or tenderness. Questionable shifting dullness was noted. The liver was palpable about 4 cm. below the costal margin and was quite tender.

There was no edema of the extremities, scrotum, or over the sacrum. Neurologic examination was negative. Rectal examination revealed no lesion.

Accessory Clinical Data.—The specific gravity of the urine was 1.029. There was a faint trace of albumin, but no sugar, and the microscopic examination showed occasional hyaline and granular casts. Erythrocyte counts on two occasions were 5.9 and 5.2 million, and the hemoglobin was 17.5 and 15 Gm. per 100 c.c. of blood (Sahli). The total and differential leucocyte counts were not remarkable. The blood nonprotein nitrogen varied from 30 mg. per 100 c.c. on admission to 47 mg. per 100 c.c. two days prior to death. The blood sugar on admission was 97 mg. per 100 cubic centimeters. The total serum protein two weeks after admission was 5.4 Gm. (albumin, 3.5 Gm., globulin, 1.9 Gm., albumin-globulin ratio, 1.8:1). At this time the icterus index was 25 units. The blood chlorides were 73 meq. per liter one week after admission, but, after intravenous fluid therapy, were 94 meq. per liter. The blood cholesterol was 273 mg. per 100 c.c., and the blood Kahn reaction was negative.

The electrocardiogram revealed normal sinus rhythm at a rate of 136, and slight left axis deviation. The P-R interval was 0.16 second, and QRS, 0.06 second; S-T_1 and S-T_4

were depressed; S-T_3 was elevated; T_1 and T_4 were upright; and T_2 and T_3 were inverted. Diagnosis: Sinus tachycardia. The record suggested myocardial disease with fairly recent myocardial infarction, probably of the posterior type.

Fluoroscopic examination of the chest showed marked cardiac enlargement due to hypertrophy and dilatation, without characteristic configuration. The amplitude of the cardiac contractions was greatly reduced. The fluoroscopic examination was repeated three weeks after admission, but no change was seen. Gastrointestinal roentgenologic studies two weeks after admission were negative. The basal metabolic rate +27 per cent. The venous pressure soon after admission was 30 cm. of saline. The circulation time (arm-to-tongue, using calcium gluconate) was 45 seconds, and the vital capacity was 2.25 liters.

Clinical Course.—The patient was given digitalis and, later, squill (Urginin). He continued to complain constantly of severe nausea, and vomited frequently. The pulse rate never fell below 116 per minute, and he continually had a pulse pressure of only 10 to 20 mm. of mercury.

On April 10, 1943, all oral medications except sedatives were discontinued without change in the patient's condition. On April 17, he began to show pitting edema over his sacrum, and, on April 19, of his ankles. Because there was evidence of ascites, abdominal paracentesis was performed; this yielded only 100 c.c. of thick yellow fluid, which congealed within fifteen minutes. The specific gravity of this fluid was 1.014.

The patient began to expectorate bright red blood on April 23, and, on April 25, his temperature rose to 38.5 C. The blood pressure had fallen slowly since admission, and was 116/100 at this time. The next day he complained of pain in the right side of his chest, and showed marked tenderness to percussion over the right hemithorax anteriorly from the costal margin to the precordium. Râles had been heard over the lower lobe of the right lung, and signs of consolidation appeared in that area. A diagnosis of infarction of the lung was made because of signs of consolidation plus marked tenderness over the area.[14] Salyrgan and aminophylline were given intravenously without effect.

Because of the persistent nausea and vomiting, fluids were given parenterally, with large amounts of thiamine hydrochloride and liver extract intramuscularly. The nausea and vomiting were constant complaints. At times the patient became quite irrational. Relief was obtained only by sedatives.

On April 27, 1943, he became unable to void, and catheterization was necessary. Edema had become severe, but the lungs were relatively clear except for the signs of consolidation in the lower half of the right lung.

On the morning of April 29, 1943, the patient's pulse became small and rapid, and the blood pressure was imperceptible. He was irrational, covered with cold clammy sweat, and presented a picture of peripheral and central circulatory collapse, with pulmonary edema. Only terminally did the patient develop any orthopnea; until then he was able to lie relatively flat in bed without respiratory distress. The pulmonary edema became more severe, and the patient died at noon on April 29, 1943.

The autopsy observations were as follows: The peritoneal and right pleural cavities contained, respectively, 1,350 and 700 c.c. of straw-colored, clear fluid with a specific gravity of 1.015. Several infarcts were found in the lower lobe of the right lung, and ante-mortem blood clots occluded the lumina of the pulmonary arteries which supplied these areas. The liver, which weighed 1,650 grams, was congested. The heart weighed 450 grams. The chambers of the right side were dilated, and the wall of the left ventricle was hypertrophied. The homogeneous gray color of the subendothelial tissue of the left ventricle was in striking contrast to the reddish-brown color of the inner surface of the right ventricle. A mural thrombus 2.5 cm. in diameter was attached to the left anterior wall, and the musculature in that area was softened and dark brown in color. Section of the left ventricular wall revealed a thin subendothelial zone and extensive patchy areas of fibrosis involving especially the interventricular septum and the posterior wall. Examination of the coronary arteries revealed numerous atherosclerotic plaques which had produced varying degrees of narrowing of the lumina of these vessels. The right main coronary artery contained a fresh thrombus which completely occluded its lumen 2 cm. from its orifice at the sinus of Valsalva.

On microscopic examination, the kidneys, adrenal glands, pancreas, and myocardium showed marked arteriolar sclerosis. The mural thrombus was in an early phase of organization. The subendothelial tissue of the myocardium was swollen and hyalinized. Focal areas of fibrosis of variable maturation, and acute and chronic inflammatory reactions were evidence of repeated occlusions of small branches of the coronary arteries. The older and

more extensive fibrosis was seen in the posterior wall and in the interventricular septum. Typical arteriolar sclerosis, with an occasional area of thrombosis, was found. The coronary arteries showed all degrees of arteriosclerosis, with luminal narrowing and finally thrombosis.

DISCUSSION

One is impressed with several features of this case which, in our experience, are not infrequent as sequelae of coronary thrombosis. These features are essentially myocardial infarction, manifested mainly by protracted nausea and vomiting. After this there was progressive cardiac insufficiency over a period of approximately two months, and the symptoms were predominantly gastrointestinal in nature and resisted all therapy.

Interesting, too, were the persistently high diastolic blood pressure and low pulse pressure, which led one to suspect pericardial effusion or constrictive pericarditis. Furthermore, the patient's entire course was characterized by evidence of "forward failure," and only terminally was there much evidence of congestive failure.

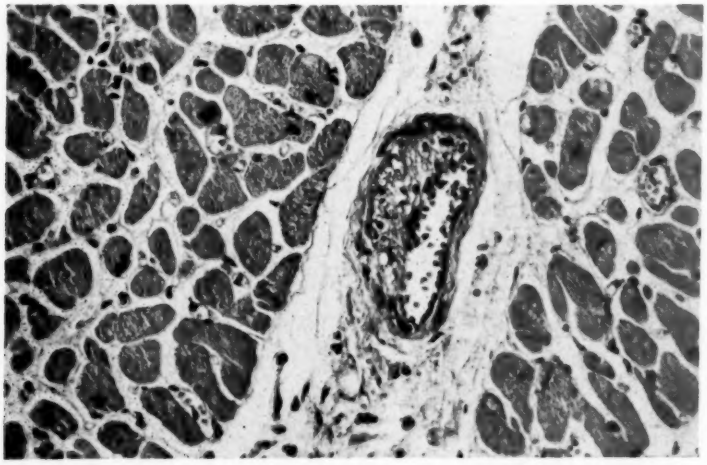

Fig. 1.—A section through apparently normal mycocardium. In the center of the photomicrograph is a small artery which shows localized thickening of the subendothelial connective tissue.

The usual causes of vomiting and nausea in a case of congestive heart failure are: (1) drugs, (2) visceral congestion, (3) vitamin deficiencies, (4) stimulation of the vomiting center by metabolites, as in uremia, and (5) extensive myocardial damage, as with the myocarditis of acute rheumatic fever. In the case presented here the nausea and vomiting were not produced by drugs such as digitalis or opiates, for the symptoms occurred prior to their administration and persisted after their discontinuance. Nor can these symptoms be attributed to visceral congestion, for at necropsy the viscera, except for the liver, showed only minimal congestion, and, indeed, the nausea and vomiting were prominent features even before the congestive phenomena were observed. The failure to improve after parenteral vitamin therapy apparently excludes vitamin deficiencies as causes of the nausea and vomiting. However, Smith and Furth[15] have reported several cases of vitamin deficiency in which the clinical course closely paralleled this case, and this raises the question whether this case may also have been an instance of chronic deficiency of vitamin B complex, as they suggest. There was no history of any such lack in this case, how-

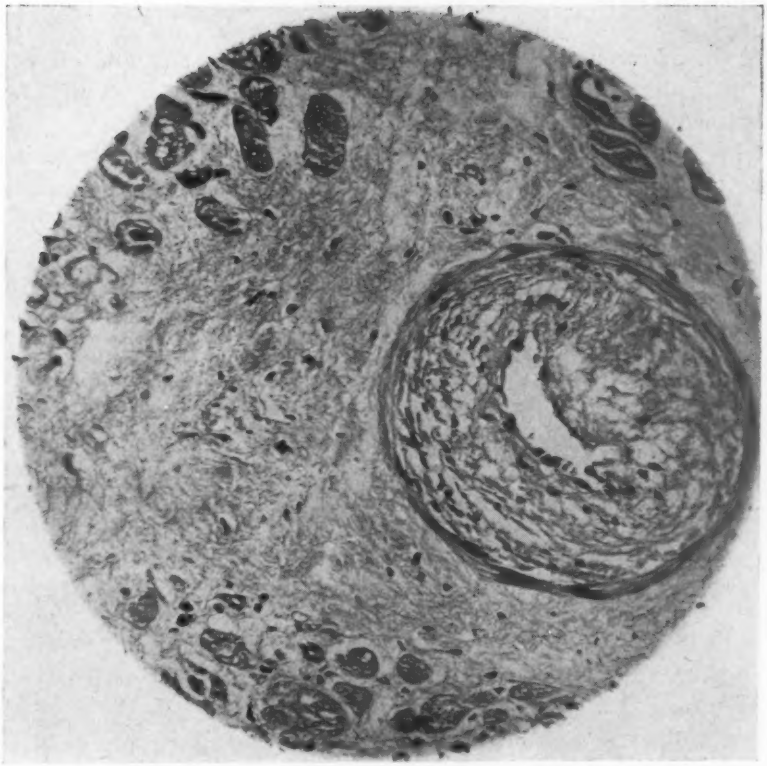

Fig. 2.—An area of myocardial scarring. At the edges of the photomicrograph, the cells are in varying stages of degeneration. The lumen of the small artery is almost completely obliterated by subendothelial connective tissue deposits.

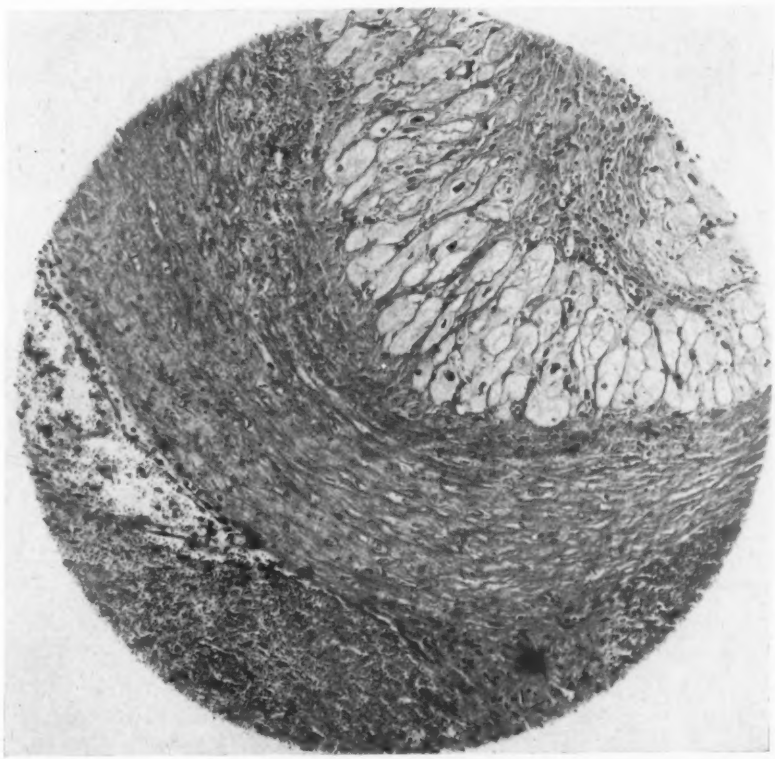

Fig. 3.—In this photomicrograph, made of a section through one of the myocardial infarctions, degenerating myocardial fibers are seen together with endocardial thickening and mural thrombosis.

ever, and, in addition, the patient received enormous amounts of vitamin B complex intramuscularly, and thiamine hydrochloride in doses of 100 to 200 mg., intravenously, on many occasions.

Hatcher and Weiss[9] found that substances formed in the body in disease may raise the excitability of the vomiting center to a level where afferent impulses which are ordinarily of subliminal value may initiate the reflex. Since, however, vomiting is rare in cases of severe anoxia due to chronic pulmonary disease, as well as in those with severe "forward failure" due to constricted hearts, it seems unlikely that in this case the above mechanism was of major importance.

From the necropsy notes and photomicrographs (Figs. 1, 2, 3, and 4) it is apparent that the essential abnormalities were limited to the myocardium, and in this case we believe the protracted nausea and vomiting were due to the extensive myocardial disease per se, acting through the same mechanism which is responsible for the emesis produced by digitalis and which, as Hatcher and Weiss[7] have shown, is initiated by a reflex from the myocardium.

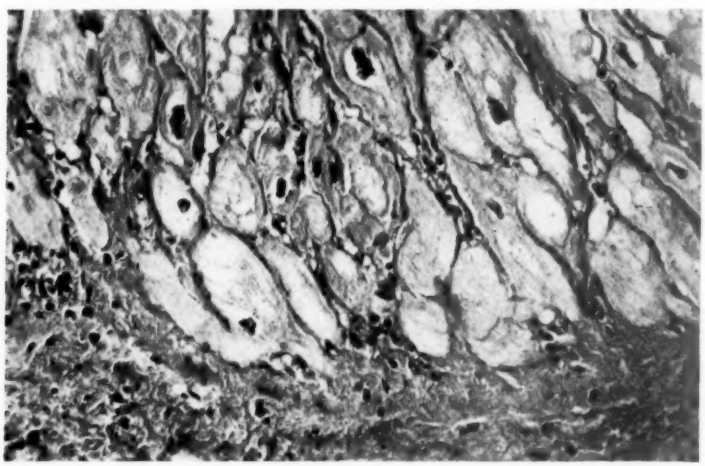

Fig. 4.—High-power photomicrograph showing acute myocardial degeneration.

Correlating the clinical and pathologic data, we assume that the following events took place: Initially, a patient with severe hypertension suffered coronary thrombosis from which he largely recovered. Subsequently, he developed another occlusion with a fall in blood pressure. Previously existing vascular disease and extensive myocardial damage combined to produce forward failure of the circulation brought about by the combination of deficient cardiac output, low arterial pressure, extremely low pulse pressure, myocardial anoxia due to low-grade coronary insufficiency, and further thrombosis of small coronary artery radicals. From this point a vicious cycle was set up, and the patient developed other smaller infarctions which led to still further coronary artery insufficiency. This combination of factors resulted in generalized myocardial anoxia. Finally, pulmonary infarctions developed which imposed an additional load on the badly weakened myocardium, resulting in terminal pulmonary edema.

It is our belief that such a slowly progressive cycle of events was the cause of the protracted gastrointestinal symptoms in this case; we further believe that the syndrome is not of infrequent occurrence, for the reports of other authors—for example, Smith and Furth[15]—are not unlike this case in many respects.

SUMMARY

The condition presented involves a patient who, after coronary occlusion, developed heart failure, the primary symptoms of which were nausea and vomiting, and in whom the significant pathologic changes were multiple areas of myocardial fibrosis. As a result of the experiences with this and other similar cases and a review of the literature, the following conclusions are drawn:

1. When nausea and vomiting are dominant symptoms in a case of heart failure, one should consider as possible factors not only drugs, congestion of the abdominal viscera, and disorders of the blood metabolites (such as occur in uremia), but should also entertain the possibility that progressive myocardial disease may be the cause of the symptoms.

2. The mechanism of the nausea and vomiting induced by progressive myocardial disease is believed to be analogous to that caused by digitalis, which has been shown to be due to a reflex arising in the heart itself.

3. When coronary thrombosis occurs in a patient with pre-existing narrowing of the smaller coronary arterial branches, a vicious cycle may ensue; the decline in cardiac output and small pulse pressure lead to further coronary insufficiency and progressive myocardial fibrosis, which bring about a further decrease in cardiac output and perpetuation of the cycle.

4. In cases of heart failure in which there is a small pulse pressure with a high diastolic pressure, the outlook is poor because of the factors outlined.

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CORONARY OCCLUSION IN INDUSTRY

A Study of Eighty-Four Cases With Reference to Subsequent Employability

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PURPOSE OF STUDY

THERE has been a definite unwillingness on the part of large industries to employ persons who are known to have arteriosclerotic heart disease or to have had myocardial infarction. This is evidenced by the employment criteria of the Eastman Kodak Company. Crain[1] states that, in 1934, this company held that a diagnosis of arteriosclerotic heart disease disqualified any man for employment. Although it is important that employers be properly safeguarded, it is equally important that persons who have recovered from myocardial infarction should be returned in so far as possible to a useful and productive position in society. Above all, they should not become dependent by reason of illness unless it is shown that the illness actually impairs their productive value. This is always important, particularly at the present time, when the armed forces are making a tremendous demand on man power, and industry must utilize all available workers.

More recently many industries have taken a less stringent view. This is in line with published studies indicating that satisfactory functional recovery frequently follows myocardial infarction.[1]

Although there are many impressions relating to the suitability or unsuitability of such persons for various types of work, there are few facts based on actual study of industrial performance. In a recent symposium on the workman's heart,[8] it was observed that the literature contained many generalities on the subject, but that the need was for a formula for physicians to work on.

This study was undertaken as a step toward providing such a formula.

The questions we seek to answer are: What proportion of persons who sustain coronary occlusion with myocardial infarction return to gainful employment? What sort of work do they do? How long do they do it? Why do they stop? If they don't return to work, why don't they?

MATERIALS AND METHOD

Eighty-four employees of the Kaiser shipyards, with a total of ninety-seven infarctions, were studied. No cases of myocardial infarction after Dec. 31, 1943, were included. Eleven patients had two separate myocardial infarctions, and one patient had three. The period of observation terminated April 20, 1944.

Cases for study were chosen by reviewing all of the electrocardiograms in the files of the Permanente Foundation Hospital. The occurrence of myocardial infarction was confirmed by subsequent perusal of the case histories.

From Medical Service of Permanente Foundation Hospitals, Oakland and Richmond, California.

Presented at the Annual Meeting of the California Heart Association, Los Angeles, May 6, 1944, and the Annual Meeting of the Western Association of Industrial Physicians and Surgeons, Los Angeles, May 6, 1944.

Received for publication Aug. 2, 1944.

TABLE I. TYPE OF WORK OF ALL PATIENTS BEFORE MYOCARDIAL INFARCTION

Manual labor	65 patients (75%)
Light or sedentary work	19 patients (25%)

The average period of observation after the occurrence of myocardial infarction was 11.7 months.

The incidence as to sex, race, and age was not remarkable.

The occupational classification was most interesting (Table I). Sixty-five patients, constituting 75 per cent of the series, performed manual labor. Only nineteen patients, or 25 per cent, could be classified as performing other than manual labor. This is particularly significant because other studies[4, 5] have been made on groups which were constituted mainly of "white collar," business, and professional people.

Follow-up study included both clinical observation and employment history.

RESULTS

Medical.—Fourteen of the eighty-four patients died during the period of study. Nine of these died immediately (within four weeks of infarction), which is an immediate mortality rate of 9 per cent for the ninety-seven infarctions.

Table II summarizes the medical status of the seventy surviving patients. Only twenty patients, a little more than one-fourth of the survivors, made a complete symptomatic recovery. Twenty-three patients, a third of the survivors, had subsequent angina pectoris. Twelve patients had congestive failure. Thirteen patients had mild degrees of angina pectoris, as well as congestive failure. There was one case of complete auriculoventricular block and one of cerebral thrombosis.

TABLE II. PRESENT STATUS OF SEVENTY SURVIVING PATIENTS

MEDICAL STATUS	WORKING	NOT WORKING	NUMBER OF CASES	PERCENTAGE OF TOTAL
Complete symptomatic recovery	10	10	20	28.6
Angina pectoris	11	12	23	32.8
Congestive failure	2	10	12	17.1
Angina pectoris and congestive failure (mild)	7	6	13	18.6
Complete A-V block	0	1	1	1.45
Cerebral thrombosis	0	1	1	1.45
Total	30	40	70	100.0

Employment.—With regard to the employment status of the seventy patients surviving at the conclusion of the study (April 20, 1944), Table II indicates that twenty were working and forty were not.

Of those patients who made a complete symptomatic recovery, ten were working and ten were not. Of the ten persons in this category who were not working, nine were unemployed because of personal reasons or some unrelated illness. Of the ten who continued at work, three went to lighter work, but seven returned to the same job they were doing before myocardial infarction.

Of the twenty-three patients who suffered from some degree of angina pectoris alone, eleven were working and twelve were not at the end of the period of observation. This is superficially comparable to what occurred among those who made a complete symptomatic recovery, but in this group those who were not employed were not working because of the angina pectoris from which they suffered.

CORONARY OCCLUSION IN INDUSTRY

A Study of Eighty-Four Cases With Reference to Subsequent Employability

Eugene B. Levine, M.D., and Edward Phillips, M.D.
Oakland, Calif.

PURPOSE OF STUDY

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Of the twelve patients with symptoms of congestive failure, two were working and ten were not. From this it appears that congestive failure after myocardial infarction is a more disabling complication than angina pectoris.

Of the thirteen patients with mild degrees of both angina pectoris and congestive failure, seven were working and six were not.

Thus, in summary, twenty persons with angina pectoris, congestive failure, or both in mild degree continued to work after recovery from myocardial infarction. It would appear that these sequelae, when sufficiently mild, are compatible with continued employment. The two patients with auriculoventricular heart block and cerebral thrombosis did not return to work.

TABLE III. INDUSTRIAL STATUS OF THIRTY WORKING SURVIVORS (43 PER CENT OF TOTAL SURVIVORS)

	NUMBER OF PATIENTS	PERCENTAGE OF TOTAL SURVIVORS
Working at same job	19	27
Manual labor	15	
Sedentary work	4	
Working at different job	11	16
Lighter physical work	6	
Sedentary work	5	

Table III summarizes the industrial status of the thirty survivors who were working at the end of the survey period. This group constitutes 35.7 per cent of the total number of patients and 43 per cent of the survivors. Nineteen of these patients returned to the same job which they held prior to myocardial infarction. Eleven returned to a different, lighter job. Thus, 27 per cent of the survivors were working at the same job they had previously held at the end of the survey period, and 16 per cent were working at a lighter job. Of those who returned to their old jobs, fifteen returned to manual labor and four returned to sedentary work. Of those who returned to lighter work, six returned to lighter physical work and five accepted sedentary positions. Table I should be compared at this point with Table III.

Of the sixty-five patients whom we studied who were doing manual labor, fifteen, or almost one-fourth, returned to manual labor. Of the nineteen patients who were doing sedentary work, only four, or about one-fifth, returned to it. Omitting altogether those persons who returned to lighter work, which would tend to weight the balance even more in favor of those previously doing manual labor, it is our observation in this relatively small series of cases that persons doing manual labor have at least as good a chance of returning to their old jobs, and certainly as good a chance of returning to some remunerative occupation after recovery from myocardial infarction, as do those persons doing sedentary work.

Table IV summarizes the industrial history of the fifty-four patients who were not working at the end of the survey period. This includes the fourteen who were dead and the forty living but not employed.

Eight patients died within four weeks after the first myocardial infarction, a mortality rate of 9.5 per cent. This figure is not significant because it obviously does not indicate the mortality rate of coronary occlusion with myocardial infarction. The only cases included in our study were those in which the patient survived long enough to have an electrocardiogram taken, or those in which the patient had myocardial infarction at some time which was not immediately recognized or diagnosed, and was recognized later by electrocardiographic study and a recheck of the history.

TABLE IV. INDUSTRIAL HISTORY OF FIFTY-FOUR NONWORKING PATIENTS (64.3 PER CENT OF TOTAL PATIENTS)

		NUMBER OF PATIENTS	PERCENTAGE OF TOTAL PATIENTS	AVERAGE TIME WORKED AFTER FIRST OCCLUSION	
Died within four weeks of first myocardial infarction		8	9.5		
Returned to work, but did not continue work, because of		26	31.0		
A. Chronic cardiac disability	15			10 Months	13 Months
B. Second myocardial infarction	5 (2 deaths)			22 Months	
C. Sudden death without coronary occlusion	1			11 Months	
D. Nonmedical reasons	5				
Failed to return to work because of		20	23.8		
A. Chronic cardiac disability	14				
B. Unrelated fracture	1				
C. Death more than four weeks after infarction	3				
D. Advice of physician	1				
E. Nonmedical reasons	1				

Twenty-six patients returned to work, but did not continue. The reasons are listed in Table IV. The great majority of these were unable to continue at work because of some cardiac disability. In three instances death terminated the work period. In eighteen, symptoms of heart disease were responsible for stopping work. Only five of these failed to continue because of nonmedical reasons. Of the twenty-one patients who returned to work, but were unable to continue because of cardiac disability of some sort, the average period of employment was thirteen months. The work period was longest among those who were forced to discontinue work by the occurrence of a second myocardial infarction, but, since this group is quite small, no conclusions can be drawn.

Twenty patients who survived more than four weeks failed to resume work after coronary occlusion with myocardial infarction. The majority of these (fourteen) continued to have disabling cardiac symptoms. The deaths of three patients occurred late, i.e., more than four weeks after the occurrence of acute myocardial infarction. One patient recovered from the symptoms of cardiac insufficiency, but was unable to return because of a fractured ankle, with complications. One patient failed to return to work because of nonmedical, personal reasons, and in only one case was a patient who recovered from symptoms of cardiac disability advised by a physician not to resume work. As a result of this advice, the patient did not request re-employment.

Analysis of the group of twenty patients who remained unemployed justifies the inference that, in this series of patients, a desire to return to work or the necessity of doing so was almost universal. Nineteen of the twenty persons who did not resume work after their first coronary occlusion failed to do so because of medical reasons, and in only one instance was a nonmedical, personal reason responsible for failure to return to some sort of work. Speculation as to whether so many would have tried to work if their income were otherwise assured is warranted, but the fact that these persons were almost forced to try to earn a living makes observations regarding their ability to do so more reliable.

Of the entire group of fifty-six patients who returned to work after their first myocardial infarction, eighteen, or 32 per cent, were able to continue

more than one year. Of the eleven patients in our series who had two myocardial infarctions, four returned to work after the second coronary occlusion. One worked eight months, and was still working at the end of the survey. Two others had worked a few months and were still employed, and one had had to stop after almost a year.

Of particular interest is the fact that ten patients worked through the critical period after coronary occlusion; they took less than one week off for the acute illness, which, for one reason or another, was not promptly diagnosed. Most of these did not consult a physician at all. The observation that some people are able to continue their normal activity, even though it is strenuous, in spite of the occurrence of acute myocardial infarction is not new. It is to be expected that, if the area of myocardium affected by the infarction is small enough, cardiac function will not be seriously impaired, and normal activity can be continued in spite of mild or even moderate discomfort. Recovery may be expected in some, if not in all, such cases. The occurrence of painless myocardial infarction is recognized, and French and Dock[9] report the case of a young soldier who was able to carry on the duties of an active military life without apparent distress in spite of extensive myocardial infarction with mural thrombus formation.

COMMENT

The relation of coronary occlusion to effort or industry is subject to some disagreement, particularly legal. Medical opinion, as expressed by Willius[10] and Master and Dack,[5] is that there is no causal relationship. Master and Dack,[5] after reviewing the histories of four hundred fifteen patients who survived acute coronary occlusion with myocardial infarction, concluded that the incidence of heart failure, subsequent infarction, or subsequent death was not any greater among those who returned to work than among those who did not.

In our series of patients it is to be expected that several who have not yet returned to work will do so in the future. Naturally, some who are working now will drop out, but, as those presently employed continue to work, the average duration of employment after myocardial infarction can be expected to rise.

It is certainly not to be expected that every employed person who suffers acute coronary occlusion with myocardial infarction, and survives, will recover sufficiently to return to work, but it is apparent that many do recover to such a degree that return to full activity may be permitted without the occurrence of any symptoms or fear of shortening life or precipitating a second coronary occlusion. Master, Dack, and Jaffe[11] report that, in a series of two hundred two patients who were followed for two to eight years, 33 per cent made a good recovery, and 50 per cent returned to work, usually at full time.

After ample time has been allowed for full recovery and the formation of a firm scar, those patients who are symptomatically well enough should be permitted to resume employment under adequate medical supervision. The work they are permitted to do should be limited only by their cardiac reserve, or, in other words, their ability to perform their tasks without untoward symptoms. Arbitrary standards governing the type of work permitted for persons who have had myocardial infarction cannot be set up, but in those industries in which medical supervision of certain groups of patients is available, the physician can, with the cooperation of the employer, return many such persons to productive labor.

It is the responsibility of the physician who is guiding the convalescence of his patient to return him, if possible, to productive work. Since it is difficult to train many people, particularly those who are doing manual labor, for an entirely different type of work, and since the number of sedentary jobs available is limited, considerable encouragement can be derived from the observation that many persons are able to return even to manual labor. Optimism regarding the work prognosis of such persons is warranted when it is seen that symptomatic recovery and an approach to normal functional capacity are proceeding satisfactorily.

The possibility of the occurrence of sudden death among persons who have angina pectoris or arteriosclerotic heart disease indicates some restriction as to the type of jobs these employees may be assigned. It would be unwise and unsafe to allow such a person to hold a position in which sudden failure of one man might endanger the life or safety of others. It would also appear unwise to permit such a person to engage in an occupation in which sudden collapse or pain might result in harm to him, either by a fall or by loss of control of machinery.

SUMMARY

Eighty-four patients who had ninety-seven myocardial infarctions before Jan. 1, 1944, were studied, of whom 75 per cent were manual laborers. The period of study ended April 20, 1944.

The average period of observation was 11.7 months.

Fifty-six patients (66.6 per cent of the total, and 73.7 per cent of those surviving four weeks) returned to work after myocardial infarction.

Thirty patients (43 per cent of the survivors and 35 per cent of all observed) returned to work and were still working at the conclusion of the period of study.

Of these, nineteen returned to the same type of work they were doing before infarction occurred.

Eleven of them returned to lighter work.

Neither angina pectoris nor slight congestive failure nor mild degrees of both prevented twenty patients from returning to gainful employment.

Only twenty (23.8 per cent) of our patients made a complete symptomatic recovery.

The probability that manual laborers may be able to resume their former employment after myocardial infarction appears to be no less than for sedentary workers.

Twenty-six patients (31 per cent of all observed) returned to gainful employment, but did not continue. Of the twenty-one who were disabled by arteriosclerotic heart disease, the average time worked after myocardial infarction was thirteen months.

Twenty patients who survived the initial critical period failed to return to work, eighteen because of heart disease.

Eighteen patients (32 per cent of those returning to work) were able to work more than one year after recovery from acute myocardial infarction.

CONCLUSIONS

The diagnosis of coronary occlusion with myocardial infarction should not of itself disqualify a man for employment or re-employment, even in a heavy industry or at manual labor. Subsequent employment should depend upon the cardiac reserve after recovery, or the ability of the patient to perform his work

without discomfort, with the restriction that such a person should not be permitted to take a job in which his sudden collapse might endanger his safety or the safety of others.

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THE RELATION OF RESTING HEART RATE TO THE INCREASE IN RATE DUE TO EXERCISE

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IT HAS been frequently assumed that there is a high positive correlation between resting heart rate and increase in rate due to exercise. During the course of experiments dealing with the reliability and validity of cardiovascular measures, it was observed that, as a rule, there was little or no relationship between resting heart rate and increase due to exercise.

Although no published reports were found in which resting heart rate was correlated with increase in rate due to exercise, data were found which were suitable for investigating this point. Jokl, et al.,[1] studied numerous physiologic responses of thirty-two South African recruits over a twenty-four-week physical training period. Their data included resting heart rates and postexercise heart rates obtained before the program began and at six-week intervals throughout the training period. The exercise which Jokl employed was forty knee bends performed in one minute. These data were adapted to our purpose by subtracting the resting heart rate from the postexercise count. Coefficients of correlation were calculated for resting heart rate and increase in rate due to the exercise for each interval at which data were secured. Five correlations were obtained: Beginning, –0.411; six weeks, –0.185; twelve weeks, –0.394; eighteen weeks, –0.377; twenty-four weeks, –0.484. In each instance it is seen that the correlation between resting heart rate and increase in rate due to exercise is negative.

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Also, data collected from five hundred forty-four college men relative to the response of the heart to exercise were available in our laboratory. The exercise employed was forty stool-steps per minute for one minute. The postexercise heart rate had been obtained by counting the number of beats for a period of two minutes immediately after the exercise. The increase in rate due to exercise was found by subtracting twice the resting rate from the postexercise count. In the case of this group of men, the coefficient of correlation for resting heart rate and increase due to exercise was found to be 0.203.

In order to obtain additional information concerning the relation of resting heart rate to increase in rate caused by exercise, data were collected from twenty college men and forty college women. To increase the reliability of the values obtained from each person, each subject came to the laboratory four times, at weekly intervals. Each time, after the resting heart rate was established for the subject in a recumbent position, he or she rode a bicycle ergometer at the rate of sixty revolutions per minute for one minute. The work performed was 1,500 kilogram-meters. As soon as the work was completed the subject resumed the reclining position. The increase in heart rate due to the exercise was found by subtracting the resting rate from the postexercise rate. The mean values for the four experiments were used in establishing the resting rate and the increase due to exercise. When these values were correlated, a coefficient of 0.281 was obtained for the men; for the women the coefficient was –0.258.

As shown by all of these experiments, there is obviously a variable relationship between resting heart rate and increase in rate due to exercise. It is of interest that, in the case of the college men, the correlation is positive, whereas, for women doing exactly the same kind and amount of exercise, it is negative. It occurred to us that the explanation of this situation might be that the relation existing between resting heart rate and the increase caused by exercise is influenced by the strenuousness of the exercise. It might be supposed that sixty revolutions of the bicycle per minute for one minute was relatively strenuous for the women, with the result that there was a negative correlation between resting heart rate and the increase caused by the exercise. In the case of the men, it might be that the positive correlation was associated with the fact that sixty pedal revolutions on the bicycle for one minute constituted comparatively moderate exercise.

In order to gain further information relative to the effect of the strenuousness of exercise on the nature of the response of the heart to exercise, additional experiments were carried out. Eighteen of the twenty college men and thirty-one of the forty college women used in the previous experiment were available. They were asked to perform exercise which was unquestionably strenuous. After a resting heart rate was established, each subject rode the bicycle ergometer at top speed for two minutes. Immediately after the exercise the increase in heart rate caused by the work was calculated as in the previous experiment. In the case of the men, the coefficient of correlation between resting heart rate and increase in rate caused by the exercise was found to be –0.731, as compared to 0.281 for the milder exercise (Table I). For the women in this experiment the coefficient was –0.460, as compared to –0.258 for the less strenuous exercise. These results confirm the belief that the more strenuous exercise is, the more negative the coefficient of correlation between resting heart rate and increase due to the exercise becomes.

It is reasonable to suppose that, if the more strenuous exercise causes the correlation described above to become more negative, light exercise should re-

TABLE I. THE EFFECT OF THE STRENUOUSNESS OF EXERCISE ON THE CORRELATION OF RESTING HEART RATE WITH INCREASE IN RATE DUE TO EXERCISE

SUBJECTS	EXERCISE	COEFFICIENT OF CORRELATION BETWEEN RESTING RATE AND INCREASE DUE TO EXERCISE
20 men	60 rev./min.	0.281
18 men	maximum /2 min.	−0.731
40 women	40 rev./min.	0.012
40 women	60 rev./min.	−0.258
31 women	maximum /2 min.	−0.460

sult in a positive coefficient. This idea was tested by having a group of forty women ride the bicycle ergometer at a rate of only forty revolutions per minute for one minute. In this experiment the coefficient of correlation between resting heart rate and the increase caused by the exercise was found to be 0.012, as compare to −0.258 for moderate exercise and −0.460 for strenuous exercise. These data further support the idea that the size and sign of the correlation between resting heart rate and increase in rate caused by exercise depend on the strenuousness of the exercise.

In seeking an explanation for the variability in the sign and size of the correlation between resting heart rate and increase in rate due to exercise, the way by which the resulting increase in minute volume is brought about must be considered. Strenuous exercise is a relative term, and from the standpoint of the individual, what is strenuous depends on his capacity to do work. It is generally recognized that, as capacity to do work increases through physical training, the resting pulse rate is reduced and the stroke volume is increased.[2]

Since this is true, the person in good condition, with a lower resting heart rate than those in poorer condition, will experience less increase in heart rate when he performs a moderate amount of exercise because he makes greater use of increased stroke volume in adjusting to the exercise. Thus, the results obtained from groups of persons of varying degrees of physical fitness doing moderate exercise show a positive correlation between resting heart rate and increase in rate due to exercise.

In order to explain the negative correlation between the resting heart rate and increase due to strenuous exercise, let us assume that the exercise is sufficiently strenuous to cause the heart to reach its maximum rate, which is approximately the same for everyone. The result is that the person with the lowest heart rate has the greatest increase, and the one with the highest resting rate will experience the least increase in rate because of the work. Under these conditions there is a negative correlation between resting heart rate and increase due to exercise.

Evidently, the correlations presented in Table I can be explained by the degree of strenuousness of the exercise which the various subjects performed. The men involved in the experiments were heterogeneous with regard to capacity to do work. For the majority, sixty pedal revolutions per minute for one minute was evidently quite moderate, but for others this work was more strenuous. The result was a small positive correlation between resting heart rate and increase in rate due to the exercise for reasons mentioned. When the men performed maximum work for a period of two minutes, the work was unquestionably strenuous for all, and the result was a high negative correlation. Forty pedal revolutions per minute for one minute proved to be quite moderate for the majority of the women, but more strenuous for some of them, depending on their capacity to do work. The result was a low positive correlation. Sixty pedal revolutions in a minute was evidently quite strenuous for the majority of

the women, and the result was a low negative correlation. When the women worked at maximum power for two minutes, the exercise was very strenuous and the result was a higher negative correlation.

CONCLUSIONS

The size and sign of the coefficient of correlation between resting heart rate and increase in rate due to exercise depend on the strenuousness of the exercise.

A group of persons whose physical condition varies from poor to good, doing mild or moderate exercise, will give either a small negative or a small positive correlation, depending on which type predominates. If the majority of them are in good physical condition, the result will be a small positive coefficient of correlation. If the converse is true the result will be a small negative coefficient.

Strenuous exercise results in a high negative correlation between resting heart rate and increase in rate caused by exercise. This is due to the fact that every person in the group approaches the maximum rate, so that those with the lowest resting rate experience the greatest increase, whereas those with higher rates experience less increase.

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ACUTE BACTERIAL ENDOCARDITIS IN THE AGED

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NEW YORK, N. Y.

INTRODUCTION

THE increasing number of men and women who attain advanced age has produced a complex series of social, economic, and medical problems. The necessary awareness of physicians is reflected in the growing list of publications on the medical aspects of old age. It is becoming apparent to the practitioner that, with the decrease in the incidence of acute infections among young people, together with improved therapeutic methods, an ever growing proportion of his patients will have passed the ages of 50 and 60 years. This situation calls for careful clinical evaluation of disease pictures in the aged in terms of present-day medicine. The study of senescence, as well as the diagnosis and treatment of disease in the aged, is a natural function of the internist. The word "geriatrics," coined in 1914, by Nascher, "to cover a special branch of medicine dealing with old age," is of great utility as a comprehensive term, but its employment should in no way obligate us to segregate a new medical specialty.

For some time the analysis and study of a large number of post-mortem examinations on persons over 60 years of age have occupied us, and have

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furnished not only valuable statistical information, but also unexpected viewpoints.[1] Among these has been the realization that bacterial endocarditis of both the acute and subacute varieties is far less rare in old persons than we had heretofore realized. We have collected from the clinical records of the Medical Services and from the protocols of the Pathologic Laboratory, covering ten years, the following groups: acute bacterial endocarditis, nine cases in patients ranging from 60 to 80 years of age; and subacute bacterial endocarditis, eighteen cases in patients ranging from 60 to 87 years of age. The age of 60 has been taken as a minimum, partly as an arbitrary, convenient point of reference and partly because by that time all persons show definite evidence of aging, although this process begins earlier in life and often is well developed before this period. The present contribution will be limited to a consideration of the cases of acute bacterial endocarditis.[2]

LITERATURE

In 1843, Graves[3] reported the occurrence in a 66-year-old man of acute endocarditis involving a bicuspid pulmonary valve. The observations of Winge[4] and Heiberg[5] established the bacterial nature of the condition, which was further clarified by Osler's "Goulstonian Lectures."[6] Lenhartz,[7] in his famous work on sepsis, published in 1903, discussed the age incidence of "septic endocarditis"; he pointed out that persons of all ages participate, and that the period of greatest frequency is between 20 and 50 years of age, but he had seen three cases in persons between 10 and 20 years, and on the other hand, four cases in persons from 60 to 70 years of age.

Thayer's classic study[8] contains a valuable statistical analysis of the age incidence of the various forms of bacterial endocarditis. "A considerable majority of the gonorrheal series occurred in individuals between 20 and 30, which corresponds, probably, fairly well to the period of greatest promiscuous sexual activity. The curve in our small influenzal series reaches its peak in the third decade. One-half the patients were under 30; one-half between 30 and 60. Influenzal endocarditis prevailed in early and middle adult life. Streptococcal endocarditis, while occurring at all ages prevailed in middle adult life. The curve for viridans endocarditis reached its peak in the third decade, that for acute streptococcal endocarditis in the fourth. The age curve of pneumococcal disease of the heart, on the other hand, is different. The rise begins in the third, reaching its peak in the fifth decade. Over 60 per cent of the patients in the pneumococcal series were over 40 years of age; 32 per cent over 50. Pneumococcal endocarditis was a disease of middle and later adult life. Staphylococcal (aureus) infections, while prevailing under the age of forty, were met with more or less indifferently throughout life."

White,[9] in his textbook, makes the broad generalization: "Acute bacterial endocarditis may occur at any age from infancy to old age." Herrmann[10] is more explicit: "Secondary type of acute bacterial endocarditis, commonly encountered in the presence of definite septic focus . . . may occur in any age group, more commonly in adults and middle-aged persons and less often in the aged and infants."

Several recent reports on acute bacterial endocarditis bear on the question of age incidence. In Ruegsegger's[11] report on pneumococcus endocarditis, four cases in patients over 60 years old are included. He points out that, whereas 50 per cent of all of his patients with pneumococcus infections were below the age of 40 years, 80 per cent of the endocarditis group were beyond this limit.

Moragues and Anderson[12] report a case of acute endocarditis due to *Pseudomonas aeruginosa (Bacillus pyocyaneus)*. The patient, a 66-year-old man, was admitted because of urinary tract infection by this organism. Repeated blood cultures showed *P. aeruginosa*, and the patient succumbed with terminal signs of acute meningitis. Although examination of the heart had been negative during life, necropsy revealed an old mitral stenosis, with a superimposed acute endocarditis. These authors list five additional cases of endocarditis due to the same organism. Of these, one[13] occurred in a man, 65 years old, following contaminated intravenous injections, and another,[14] in a man, 71 years old, was secondary to urinary tract infection.

In a Cabot case report[15] on pneumococcus endocarditis in a man, aged 64 years, meningitis again appears to have been a terminal manifestation. In a 75-year-old man suffering from acute bacterial endocarditis due to an unidentified organism, Bartol, Edwards, and Lamb[16] found a dissecting aneurysm of the aorta which arose in the base of a complicating mycotic aneurysm.

Other pertinent case reports will be discussed in the section on therapy.

TABLE I. ACUTE BACTERIAL ENDOCARDITIS IN THE AGED

CASE	AGE (YR.)	SEX	ORGANISM (BLOOD CULTURE UNLESS STATED OTHERWISE)	CLINICAL DIAGNOSIS	DURATION OF ILLNESS	PORTAL OF ENTRY	COMMENT
1	61	M	Pneumococcus, Type XXVIII (also from right sphenoid and spinal fluid)	Pneumococcus meningitis and sinusitis; diabetes	13 days	Nasal sinuses	Died 2 hours after ethmoidectomy
2	63	F	Pneumococcus, Type III	Acute mastoiditis; lateral sinus thrombosis; diabetes	70 days	Ear	Chill, fever 24 days after mastoid operation; treated with sulfanilamide
3	80	F	Pneumococcus, Type VI	Pneumonia	14 days	Lung. Carcinoma of stomach	Unsuspected carcinoma of stomach at autopsy
4	74	F	Pneumococcus, Type XI and *Streptococcus hemolyticus*	Agranulocytosis; necrosis of tonsils	17 days	Tonsils	Onset gradual 2 weeks before admission; no medication
5	62	F	*Streptococcus hemolyticus*	Diabetes; acidosis; cerebral lesion; coronary thrombosis	6 days	Not known	Stuporous on admission; kidneys showed intercapillary glomerulosclerosis
6	70	F	Anaerobic streptococci	Adenocarcinoma of uterus; pyometra	3 weeks	Pyometra	Chills and fever began 3 weeks before death
7	60	F	Enterococcus and *Staphylococcus albus*	Left ureteral calculus; pyonephrosis	18 days	Pyonephrosis	Death 4 days postoperatively
8	65	M	*Staphylococcus aureus*	Bronchopneumonia? Old coronary occl.	3 days	Infection in right toe	Sputum showed pneumococcus, Type VII
9	80	M	*Escherichia coli* from heart valve (smear from vegetation-cocci)	Bronchopneumonia	5 days	Not known	Areas of tender swelling, both external malleoli

CASE REPORTS

CASE 1.—*Pneumococcus Type XXVIII, sinusitis, and meningitis in diabetic man, aged 61 years, who died two hours after bilateral sphenoethmoidectomy. Autopsy showed acute purulent meningitis, and acute pneumococcus (Type XXVIII) endocarditis of aortic and mitral valves.*

The patient was admitted to the Mt. Sinai Hospital March 2, 1937. Eighteen months previously he had undergone splenectomy for splenomegaly and secondary anemia. Five days before admission he suffered a shaking chill, lasting one hour, and followed by a fever of 104° F. He complained of sharp pains shooting up and down his spine, pain in the lower extremities, and severe headache associated with emesis. On examination he appeared acutely ill and was delirious. The pharynx was dry, granular, and injected. Râles were heard at

the base of the left lung. The heart sounds were of fair quality; a harsh systolic murmur was heard all over the precordium. The peripheral vessels were moderately sclerotic. The abdomen showed well-healed right upper and left upper quadrant scars. The liver was palpable. The blood pressure was 140/80. The hemoglobin was 89 per cent, and the leucocyte count, 13,600, of which 88 per cent were polymorphonuclears. The urine showed a trace of albumin, 10 per cent sugar, heavy traces of acetone, and occasional hyaline casts and erythrocytes. Spinal puncture revealed a purulent fluid containing numerous gram-positive organisms, mostly diplococci. In view of the fact that meningococci occasionally may be gram-positive at first, antimeningococcus serum was administered intraspinously and intravenously. A consultant for nose and throat diseases found no evidence of suppuration in the sphenoid and ethmoid sinuses. A pneumococcus, Type XXVIII, was recovered from the spinal fluid, from the blood, and from the secretion of the right sphenoid. For this reason, exploratory bilateral sphenoethmoidectomy was performed, but no frank suppurative focus was encountered. After the operation the temperature rose sharply to 106.8° F., and patient died twenty-four hours later. The glycosuria and acidosis had been controlled by insulin.

Post-mortem examination revealed the following: acute, purulent menignitis (pneumococcus, Type XXVIII); acute pneumococcus, Type XXVIII, endocarditis of mitral and aortic valves; chronic rheumatic heart disease, mitral valve; coronary sclerosis without narrowing; a patent foramen ovale; nephrocirrhosis atherosclerotica lenta incipiens; fibroadenoma of the prostate; a colloid adenoma of the thyroid; and the status six years after cholecystectomy and one and one-half years after splenectomy.

Comment.—The portal of entry here was the accessory nasal sinuses, infection of which led to blood stream invasion, with subsequent acute endocarditis and suppurative meningitis. Noteworthy was the involvement of both mitral and aortic valves, although the pathologist found evidence of old rheumatic valvular lesions only on the mitral leaflets. The spleen, removed a year and a half before, had shown microscopic changes which were interpreted as being due to chronic infection, but there is no reason to believe that there was any connection between the antecedent splenic disease and the fatal illness.

CASE 2.—*Pneumococcus, Type III, ear infection in a 63-year-old woman with diabetes; acute mastoiditis; simple mastoidectomy and obliteration of lateral sinus because of purulent thrombosis. Twenty-four days later, chills and fever; blood culture positive for pneumococcus, Type III; reoperation and dural vein exploration; extension into opposite sinus found. At autopsy, bilateral lateral sinus thrombophlebitis, and acute pneumococcus, Type III, endocarditis of aortic valve.*

This patient, known to have diabetes, was admitted to the Mt. Sinai Hospital April 20, 1937, because of aural pain and discharge from the ear for one week, following an upper respiratory infection. At this time the diabetes was not under control. Culture of the discharge disclosed a pneumococcus, Type III, and roentgenologic examination showed mastoid involvement. Mastoidectomy revealed the extensive bony destruction which is characteristic of pneumococcus, Type III, infection. Creamy, thick pus appeared when the lateral sinus was incised. There was no bleeding from the bulbar end, and only a moderate amount from the torcular end. The patient did very well, and was out of bed walking about, when, on the twenty-fourth day after the sinus operation, she suffered a chill, and fever again set in. A blood culture disclosed pneumococcus, Type III. The patient was immediately operated on again; the internal jugular vein was ligated, and the dural sinuses were re-explored. There was evidence of extension into the straight sinus and into the opposite side. The patient died June 23, 1937.

Post-mortem examination revealed the following: bilateral lateral sinus thrombophlebitis; acute pneumococcus, Type III, endocarditis, aortic valve; chronic rheumatic disease, mitral and aortic valves; coronary sclerosis, without narrowing; pulmonary emphysema; generalized arteriosclerosis; and obesity.

Comment.—This patient illustrated the characteristic course of pneumococcus, Type III, infections of the mastoid, which have so long baffled the otologists. Here, too, the endocarditis was clearly secondary to blood stream infection following mastoid and lateral sinus infection. Old rheumatic valvular lesions were present. The administration of sulfanilamide at time of the first

operation was not effective in clearing up the infection. The action of these drugs in cases of ear disease, in which they often cause temporary improvement and thus promote a false sense of security, has been pointed out by Maybaum, Snyder, and Coleman.[17]

CASE 3.—*Daily shaking chills and pyrexia in a woman, aged 80 years; cause obscure until, on eleventh day of illness, the second blood culture contained a pneumococcus (Type VI). Sulfapyridine therapy caused thrombocytopenic purpura and skin eruption. Died thirteen days after first chill. Post-mortem examination: acute pneumococcus (Type VI) endocarditis, mitral and aortic valves, with perforation of anterior mitral and left aortic cusps.*

The patient was admitted to the Mt. Sinai Hospital Nov. 20, 1940, with the history that seven days before she had noted nausea and emesis without obvious cause, and five days before had had a shaking chill with a temperature rise to 103° F. Thereafter chills occurred daily. Examination revealed obesity, deafness, fever, evidence of right-sided iridectomy for glaucoma, pulmonary emphysema, crackling râles at the bases of both lungs, a high-pitched, rough systolic murmur at both aortic and mitral areas, and a distended abdomen. The hemoglobin was 80 per cent, and the leucocyte count, 8,600, of which 56 per cent were segmented, 25 per cent nonsegmented, 12 per cent lymphocytes, 6 per cent monocytes, and 1 per cent, basophiles. The urine was clear and acid, and contained a trace of albumin and occasional granular and cellular casts. The blood urea nitrogen was 37 mg., and the cholesterol, 210 milligrams. The first blood culture was sterile. The second (Nov. 26, 1940) showed pneumococcus, Type VI. Excretion pyelograms were normal. A roentgenogram of the chest showed numerous miliary and submiliary infiltrations of the lower two-thirds of the right lung, and an irregular area of density in the left lower lobe behind the heart, probably an area of consolidation. A barium enema showed nothing abnormal. An electrocardiogram revealed no significant change. Sulfapyridine therapy was started on admission, but did not affect the septic temperature curve. On the sixth day after entry an erythematous rash appeared on the trunk and left upper extremity. In addition, a number of purpuric spots were noted in the conjunctivae. The blood platelets had dropped to 50,000. Because of the thrombopenia, the sulfapyridine was discontinued, and the patient was given antipneumococcus, Type VI, rabbit serum. The patient died two days later.

At autopsy the following diagnoses were established: acute pneumococcus (Type VI) endocarditis of mitral and aortic valves, with perforation of anterior mitral and left aortic cusps; acute focal myocarditis at point of contiguity with mitral vegetation; chronic rheumatic heart disease, mitral valve; carcinoma of stomach; large, benign, prepyloric polyp; embolus in superior mesenteric artery; and marked sclerotic narrowing of the ostium of the celiac axis.

Comment.—The portal of entry of the infection in this case could not be established with certainty. Both the lungs and the clinically unsuspected carcinoma of the stomach must be considered. Here we may speak of a primary, or idiopathic, endocarditis in which the signs of blood stream infection far overshadowed the localizing manifestations. The association of the gastric neoplasm with a benign prepyloric polyp is of interest from the standpoint of the metaplasia of benign lesions in the gastrointestinal tract.

CASE 4.—*Cryptogenic agranulocytosis of nineteen days' duration in a woman 74 years old, associated with mixed infection of the blood stream by a pneumococcus, Type XI, and Streptococcus hemolyticus, probably secondary to gangrenous pharyngitis and tonsillitis. Post-mortem examination: bacterial endocarditis of pulmonary, mitral, and aortic valves.*

The patient was admitted to the Mt. Sinai Hospital April 9, 1934. She had been in relatively good health until two weeks before admission, when fever, sore throat, and weakness were noted. No medicine of any kind had been taken. There had been no chills. Physical examination disclosed that the pharynx was red and congested, and the tonsils large, swollen, and covered with easily removable grayish-white membrane, removal of which caused no bleeding. The upper anterior cervical nodes were large and tender. The heart, except for numerous extrasystoles, exhibited no abnormalities. The lungs were hyperresonant; the expiratory phase of respiration was prolonged, and numerous sibilant and sonorous râles were heard. The hemoglobin was 68 per cent, and the leucocyte count, 1,900, with 98 per cent lymphocytes and 2 per cent monocytes.

Therapy with liver extract, 2 c.c. intramuscularly every four hours, was started at once, and 500 c.c. of whole blood were transfused. The patient died on the third day after admission. A blood culture taken on the evening of her death revealed *Streptococcus hemolyticus* and a pneumococcus, Type XI. At no time was acute bacterial endocarditis suspected.

Post-mortem examination disclosed acute bacterial endocarditis involving the pulmonary, aortic, and mitral valves; necrosis of the soft palate and tonsils; chronic rheumatic valvular disease, mitral; generalized arteriosclerosis; and healed fibroid tuberculosis, with a primary complex and a calcified hilar node.

Comment.—The breakdown of the defensive mechanisms in agranulocytosis is well known. The occurrence of a mixed infection is therefore not surprising. The pre-existing rheumatic valvular lesion (mitral) again seemed to determine the localization on the heart valves.

CASE 5.—*A woman, 62 years old, had diabetes; for two months, dyspnea and precordial pain on exertion; for three days before admission, nausea, emesis, epigastric pain, and extreme weakness; and for two days was irrational and stuporous. Diabetic acidosis was apparent, but whether a cerebral lesion, coronary thrombosis, or acute pyelonephritis was the cause of other symptoms was not clear. Patient died on second day in hospital. Blood culture reported posthumously revealed Streptococcus hemolyticus. Autopsy: acute streptococcus endocarditis, mitral valve.*

The patient had suffered for thirteen years from diabetes, for three years from tinnitus, vertigo, and scotomas, and for three months from progressive dyspnea on exertion and moderate weakness. For two months she had had attacks of precordial pain radiating to right arm, associated with dyspnea. For three days before admission, nausea, epigastric pain, emesis, and weakness had been present; for two days she had been stuporous and irrational. On examination, the temperature was 100.8° F., the pulse rate, 120, the respirations, 25, and she was dyspneic and stuporous. The heart sounds were poor in quality; a harsh systolic murmur was heard maximally at the apex. The blood pressure was 180/110. The hemoglobin was 85 per cent, and the leucocyte count, 19,000, of which 90 per cent were polymorphonuclears. The urine contained sugar (5.8 per cent), acetone (2 plus), albumin (2 plus), numerous leucocytes, occasional erythrocytes, and hyaline casts. The blood sugar was 325 mg., and the carbon dioxide combining power, 24 volumes per cent. The electrocardiogram revealed changes indicative of marked myocardial damage. At first the patient was believed to have had acute coronary thrombosis, which, in turn, led to diabetic acidosis. On the other hand, pyelonephritis with an associated bacteremia was considered as a factor in the causation of the acidosis. Progressive clouding of the sensorium, the development of bilateral Babinski signs, and generalized areflexia suggested the possibility of a cerebral lesion. Saline and glucose with insulin, intravenously, raised the carbon dioxide combining power to 47 volumes per cent. Lumbar puncture revealed clear fluid. The temperature rose steadily, and the patient died on the second day after admission. A blood culture, reported posthumously, showed *Streptococcus hemolyticus.* At no time was bacterial endocarditis considered as a diagnostic possibility.

Autopsy showed acute *Streptococcus hemolyticus* endocarditis, mitral valve; coronary arteriosclerosis, with marked narrowing; myocardial fibrosis, myocardial abscess; generalized arteriosclerosis; acute and chronic cystitis; and intercapillary glomerulosclerosis.*

Comment.—The portal of entry in this case is not clear, and one might be justified in placing it in the primary, or cryptogenic, group, were it not for the cystitis found at autopsy. The occurrence of diabetes makes a total of three such cases out of the nine reported in this paper.

CASE 6.—*Woman, aged 70 years, with malignant neoplasm of uterus (associated with foul vaginal discharge for about eight months) which was found inoperable. For four weeks frequent shaking chills with high fever; first blood culture sterile, but one done four days before death contained anaerobic streptococci. Post-mortem examination: acute streptococcus endocarditis, mitral valve.*

For eight months this patient, whose past history was essentially negative, had suffered from a foul vaginal discharge, but vaginal bleeding had been noted for only one day. On Oct. 24, 1932, she was admitted to the Mt. Sinai Hospital, where a large, hard, firm, smooth mass

*This patient is included among the cases reported by Allen, A., and Siegal, S.: Intercapillary Glomerulosclerosis, Am. J. M. Sc. 201: 516, 1941.

could be felt reaching halfway to the umbilicus. Because of skin ulcers caused by the application of heat to the abdomen, the patient was discharged to allow for healing of the skin. She returned six weeks later with the skin healed, and reported a gain of 4 pounds in weight. However, a week before admission, she suffered a shaking chill, with temperature elevation to 103° F. This recurred the next day. Both urine examination and blood culture showed no cause for fever. At laparotomy an inoperable carcinoma of the body of the uterus was found. On the fourth day after operation a chill occurred, and during the next two weeks the patient had five chills, with temperature elevation to 104° F. The urine at no time showed pus. On the seventh day after operation a large, left subconjunctival hemorrhage was noted. A blood culture taken four days before death showed anaerobic streptococci. The clinical diagnosis was carcinoma of the uterus, and pyometra.

Post-mortem examination disclosed adenocarcinoma of the corpus uteri, with necrosis and suppuration; carcinomatous infiltration of the parametria, right ovary, and right ovarian veins; acute streptococcus endocarditis, mitral valve; and suppurative infarct of the spleen.

Comment.—This patient illustrates association of infection with a neoplasm in which the relationship was clear. At times infection may completely mask an underlying neoplasm. The endocarditis was of the secondary type, without a demonstrable pre-existing valvular lesion.

CASE 7.—*Woman, aged 60 years, had left loin pain of two weeks' duration, and had had similar attacks fifteen, and one and one-half, years before; diagnosis of left calculus pyonephrosis made after urologic studies. After cystoscopic examination, blood culture showed enterococcus and Staphylococcus albus. At operation, left kidney with the calculus was removed. Patient died on fourth day after operation. Autopsy: acute bacterial endocarditis, mitral valve.*

Because of left loin pain of two weeks' duration, similar to attacks fifteen, and one and one-half, years before, this 60-year-old woman entered the hospital. Obstipation for three days, ineffectual enemas, emesis, and abdominal distention suggested ileus, but roentgenologic examination showed no organic obstruction, and the bowels eventually moved with enemas. The blood pressure was 170/64. The heart was enlarged and a systolic murmur was heard at the apex. Urologic studies showed a nonfunctioning left kidney, and obstruction was encountered at ureteropelvic junction. After the last cystoscopic examination a chill and temperature rise occurred. A blood culture revealed both enterococcus and *Staphylococcus albus.* Urine culture also showed *Staphylococcus albus.* Because of the presence of calculus pyonephrosis with bacteremia, nephrectomy was performed and the diagnosis confirmed. Postoperatively the patient did poorly; she developed a stiff neck and a bilateral Kernig sign. The spinal fluid was clear and contained only six lymphocytes, but *Staphylococcus albus* was cultured from it. The patient died on the fourth day after operation. At no time was acute bacterial endocarditis suspected.

Post-mortem examination disclosed acute bacterial endocarditis, mitral valve, due to mixed infection; abscesses, right kidney; and parenchymatous degeneration of heart and kidney.

Comment.—Acute endocarditis, secondary to calculus pyonephrosis, was here associated with a mixed infection of the blood stream (enterococcus and *Staphylococcus albus*). This occurrence has recently been emphasized by Orgain and Poston,[18] and will be discussed later in this report in connection with Case 4.

CASE 8.—*Man, aged 65 years, with sudden onset of chills and fever six months after myocardial infarction; thought to have bronchopneumonia; blood culture showed Staphylococcus aureus; died three days after onset. Autopsy: acute staphylococcus endocarditis, mitral valve; severe coronary sclerosis, with narrowing.*

Six months before, this patient had been treated at the Mt. Sinai Hospital for myocardial infarction. He had done well until six hours before admission, when pain in left hemithorax came on suddenly and was followed by a shaking chill. On examination, signs suggestive of bronchopneumonia were noted at the base of both lungs. The heart sounds were of fair quality, with a blowing systolic murmur at the apex. The blood pressure was 105/40. The hemoglobin was 92 per cent, and the leucocyte count, 17,600, with 82 per cent polymorphonuclears. The blood urea was 11 milligrams. The electrocardiogram showed evidence of previous myocardial infarction of the posterior wall. The temperature, which on admission was 103° F., rose sharply in a few hours. Sputum culture disclosed pneumococcus, Type VII.

A blood culture taken at that time was reported thirty-six hours later to contain *Staphylococcus aureus*. The following day an area of redness was noted on the lateral aspect of the right big toe, and two lymphangitic streaks appeared on the dorsal aspect of the foot. There were no petechiae and no evidence of superficial thrombophlebitis. The right dorsalis pedis pulsation, noted as present on admission, became imperceptible. On the day of death, three days after the onset, a bluish, tender discoloration on the palmar aspect of the left hand developed at the base of the metacarpal bones.

Post-mortem examination revealed: acute *Staphylococcus aureus* endocarditis, mitral valve; subacute, incomplete closure of the right coronary artery due to hemorrhage in a plaque; extensive arteriosclerotic narrowing of left circumflex and left anterior descending coronary arteries; acute myomalacia of the posterior wall of the left ventricle; arteriosclerosis of the aorta; acute infarction of the right kidney; and multiple excretion abscesses in both kidneys.

Comment.—A true primary, or cryptogenic, endocarditis was present in this case. The sputum culture would seem to indicate that bronchopneumonia, possibly secondary to congestive heart failure, was due to pneumococcus, Type VII. The blood culture, containing *Staphylococcus aureus*, came as a distinct surprise. The endocardial implant occurred on an otherwise normal valve. A similar case was reported recently in which a 35-year-old woman had suffered from a pneumococcus, Type I, pneumonia and empyema, and at autopsy was found to have a *Staphylococcus aureus* bacteremia and acute staphylococcus endocarditis of the mitral and pulmonary valves.[19]

CASE 9.—*Man, aged 80 years, had gradual onset of pain in right external malleolus and fever for three days; he was moribund on admission, and no diagnosis was made. Autopsy: acute bacterial endocarditis, mitral valve, organism unknown.*

After prostatectomy two years before, this 80-year-old man had occasional hematuria, but was otherwise well until two weeks before admission to the Mt. Sinai Hospital, when he had an attack of so-called indigestion and was in bed for three days. One week before admission he developed pain in the region of the right external malleolus, with pain on motion and redness; two days later there were cough and fever. The patient was in extremis. He was restless and uncooperative, with a clouded sensorium; the pharynx was red and swollen; the chest was barrel shaped, and there were dullness and diminished voice and breath sounds over the lower half of both lower lobes, with numerous medium and coarse moist râles. The cardiac outlines could not be ascertained; the sounds were of very poor quality. Peripheral arteriosclerosis was marked. The blood pressure was 154/82. Abdominal distention interfered with palpation of the viscera. An area of erythema over both external malleoli was observed. He died twelve hours after admission.

Post-mortem examination revealed acute bacterial endocarditis, mitral valve; acute and chronic bronchitis, pulmonary emphysema, bronchopneumonia of left upper and left lower lobes; general arteriosclerosis; and multiple petechiae in the kidneys and ureters. Culture of the vegetation yielded pure *Escherichia coli*, although, on direct smear, many gram-negative rods and gram-positive cocci were seen. The bacteriologic observations therefore permitted no definite interpretation.

Comment.—This case shows how difficult clinical diagnosis can be when the patient is moribund when he is seen for the first time. Autopsy revealed acute endocarditis, but we are entirely in the dark as to its pathogenesis and the causative organism, although the bronchopneumonia must be considered as a possible primary focus.

PATHOLOGY

For a general description of the pathology of acute bacterial endocarditis, the reader is referred to the textbooks of Aschoff, Kaufmann, and MacCallum, and to the monograph of Libman and Friedberg[21] for a comprehensive discussion of the pathologic changes in subacute bacterial endocarditis, with particular emphasis on the differentiation between the two forms. At this point it is our purpose simply to point out certain outstanding pathologic features of our cases.

The valvular lesions consisted of the typical, large, friable vegetations in which freshly made smears showed masses of bacteria. The mitral valve was involved in all but one case (Case 2), and in five cases was the only one involved. The aortic valve was involved alone in one case (Case 2), together with the mitral valve in two cases (Cases 1 and 3), and with the mitral and pulmonary valves in one case (Case 4). In Case 3 both the anterior mitral and the left aortic cusps were perforated by the inflammatory process, giving rise to the picture of what the older pathologists termed "ulcerative endocarditis." At the point where the vegetation on the under side of the mitral valve came in contact with the lateral wall of the ventricle there was a localized area of endocardial inflammation, with involvement of the underlying myocardium.

In four out of the nine cases, definite, old rheumatic lesions involving the mitral valve were found. In one of these (Case 2) the aortic valve was similarly involved. In spite of the age of the patients in this series, in only one (Case 8) was there any arteriosclerotic thickening of the valve. In four of the nine cases no previous valvular damage of any kind could be found.

As to the occurrence of embolic phenomena, in three cases (Cases 1, 6, and 7) there were none. In Case 2 there was microscopic evidence of acute myocarditis. In Case 3, embolism of the superior mesenteric artery was found; this had apparently occurred shortly before death. In Case 5 a myocardial abscess was found, and examination of the brain revealed toxic encephalopathy. Kernohan, Woltman, and Barnes,[20] in discussing involvement of the central nervous system in association with endocarditis, have pointed out that "changes in the central nervous system with or without clinical symptoms are not only common to all types of endocarditis, but also are distinctive." Case 8 was the only instance in the series of multiple excretion abscesses of the kidneys. The embolic lesions of the skin will be taken up in connection with the discussion of the clinical picture.

In a group of aged persons, the significance of the associated conditions cannot be overemphasized. By this we do not mean such manifestations as the meningitis in Case 1, the latent sinus phlebitis in Case 2, or the carcinoma of the uterus in Case 6, for these conditions are to be regarded as part of the chain of events definitely leading to sepsis. In four cases (Cases 4, 5, 8, and 9), diffuse gross arteriosclerosis was present. In Case 3, arteriosclerotic narrowing of the ostium of the celiac axis was found, in addition to an undiagnosed malignant neoplasm of the stomach and a benign polyp of the stomach. In Case 5, the kidneys were the seat of the lesion now known as intercapillary glomerulosclerosis; in addition, there were marked narrowing of the coronary arteries and myocardial fibrosis. In Case 8, myocardial infarction due to coronary thrombosis occurred six months previously, with consequent functional impairment. In Case 9, both acute and chronic bronchitis were found. To what extent these conditions, especially the generalized arteriosclerosis and the arteriosclerosis of the coronary vessels, influenced the clinical picture cannot be stated definitely, but it may be fairly assumed that these abnormalities do reduce the functional capacity of the tissues and the organs, and of the body as a whole. We believe that it is changes such as these that make the clinical picture of disease in the aged different from that in the young, for in the latter group the tissues and organs are unaltered either by associated diseases or the processes of senescence. In other words, if a disease picture is the result of the interaction of a pathogenic organism and the defense mechanisms of the human body, the variables are the virulence of the organism and the reactive power of the body, which in youth

is unhampered by the added burdens so common in later years. Three of the nine patients, for example, suffered from diabetes mellitus, and two of these had diabetic acidosis on admission to the hospital.

BACTERIOLOGY

Pneumococci of various types were cultured from the blood in four of the nine cases. In one of these a hemolytic streptococcus was also found. By including the enterococcus in the streptococcus group, we find that this species was also recovered in four cases, of which two were the hemolytic variety. *Staphylococcus aureus* occurred in one case, and, in another, *Staphylococcus albus* was associated with the enterococcus. It will be recalled that both Ruegsegger[11] and Thayer[8] emphasized the occurrence of pneumococcus endocarditis in the higher age groups. The latter also pointed out that staphylococcus endocarditis, although it occurs at all ages, was most common in the third and fourth decades.

In connection with the two cases of mixed infection, we call attention to a recent contribution by Orgain and Poston,[18] in which they report six patients with bacterial endocarditis from the blood of whom they repeatedly cultured two or more distinct species of bacteria. There was little in the history, physical and laboratory data, and clinical course of their patients to suggest a mixed infection. They emphasize that recognition of a mixed infection is of fundamental importance in sulfonamide therapy, for the drug may affect one organism and not the other.

The difference in the bacterial content of the blood stream and the sputum is noteworthy in Case 8, in which the sputum yielded pneumococcus, Type VII, and the blood, *Staphylococcus aureus*. A similar situation was recently reported from Boston,[19] and was mentioned in the comment on Case 8. A woman, aged 53 years, died, as it semed, from pneumococcus, Type I, pneumonia, and empyema. Post-mortem examination disclosed, in addition, acute staphylococcus endocarditis and bacteremia.

The portal of entry of the infective agents was clear in five cases of this series, questionable in two, and not known in two. The clear origins of the bacteremia were acute nasal sinusitis, middle ear infection and mastoiditis with sinus phlebitis, agranulocytosis with gangrenous mouth lesions, pyometra, and pyonephrosis. In the dubious cases the bacteremia may have originated either in the lungs or a gastric neoplasm in one instance, and, in the other, in an infection of the great toe, which was more likely a result than a cause of the sepsis. In the remaining two cases (Cases 5 and 9) no portal of entry could be recognized with certainty.

CLINICAL PICTURE

In none of these nine cases was the correct diagnosis made, or even suspected, ante mortem, in spite of the demonstration of bacteremia in several. The continuing fever and progressive downward course of the patient were often ascribed to the obvious presenting condition, as in Case 7, in which the infected adenocarcinoma of the uterus seemed an adequate explanation for the observed symptoms and signs. In Case 5 the clinical manifestations were explained as the result of one of several possible conditions, i.e., diabetic acidosis, coronary thrombosis, or cerebral hemorrhage. In Case 8 the easily detected bronchopneumonia due to pneumococcus, Type VII, seemed an adequate diagnosis until *Staphylococcus aureus* was found in the blood stream. In general, the multiplicity of lesions causing symptoms and physical signs in the aged accounts for

many of the diagnostic difficulties. The keenest discrimination is required to avoid misplacing clinical emphasis. In many of the cases reported, the urgency of certain aspects, such as diabetic acidosis, tended to distract attention from the problem as a whole.

Table I shows that five cases occurred in the seventh decade of life, and two each in the eighth and ninth. The striking difference in sex incidence (six females to three males) is not easily explained. It may well be due only to the small number of cases, but it should be considered along with other well-known sex differences of later life, such as the greater longevity, the lower incidence of arteriosclerotic heart disease and malignant neoplasms, and the greater mental stability, of the aged female.

Among the conditions arising to confuse the clinician in these cases may be noted the difficulty in the interpretation of the cardiac manifestations. In old patients with frank chronic valvular disease, even more often than with the young, no history of previous heart disease or of attacks of rheumatic fever can be elicited, and such was the case here. Yet, as has been shown in the discussion of the pathologic changes, in four, and possibly five, of nine cases there were definite old valvular lesions, presumably of rheumatic origin. Only one patient showed definite arteriosclerotic valvular changes. If we review the clinical records, we find that in three of the four cases of proved rheumatic disease there were harsh systolic murmurs, either at the mitral or aortic areas, or these murmurs were loud over the entire precordium. In the remaining rheumatic case the only observed cardiac abnormality was the occurrence of extrasystoles. In Case 5 a harsh systolic murmur was audible, and, at autopsy, fibrosis of the myocardium due to arteriosclerotic narrowing of the coronary arteries and dilatation of all the heart chambers were found. It is clear that the interpretation of the auscultatory phenomena in these ailing old people presents great difficulties. In general, we believe that systolic cardiac murmurs in the aged may be due to rheumatic valvular deformities, arteriosclerotic valvular lesions, including calcification of the valves and of the mitral ring (not observed in the present series), and to cardiac dilatation. Systolic murmurs which appear acutely may be caused by perforation of a valve cusp or by rupture of a papillary muscle. The differentiation is impossible without careful study of both the history and the physical signs, plus the aid of the roentgenologic examination, which may be used to detect valvular deposits of calcium, as well as variations in the size of the heart. These observations refer largely to involvement of the mitral valve. Lack of space precludes discussion of the signs of aortic stenosis, either with or without calcification—a lesion that is far from rare in the aged and which has been thoroughly discussed by many writers in the past ten years. That no change in the character of the heart sounds and murmurs in this series of cases was noted means only that insufficient attention was paid to this point.

Since in cases of both acute and subacute bacterial endocarditis, clinicians have long been trained to look for embolic skin lesions, their occurrence in this series deserves discussion. In Case 4, petechiae were noted after an eruption thought to be due to sulfonamides had subsided. In Case 6 a large subconjunctival hemorrhage appeared once during the course of the disease. In Case 8 a tender red area was noted on the right big toe, and a similar area of redness over the right external malleolus occurred in Case 9. It is our belief that the paucity of embolic skin lesions is to be ascribed to faulty observation, rather than to any peculiarity in the disease or to the age of the patients. These manifestations must be looked for daily and with meticulous care. The petechiae in subacute bacterial endocarditis may be very elusive even in clear-cut cases. It

is obvious that, when the possibility of endocarditis is unsuspected, little time will be given to looking for skin lesions.

It may be urged by some that acute bacterial endocarditis in the aged is a "terminal" or "agonal" manifestation. We believe rather that it may be at times a "terminating" condition, since no one can deny that, in some of these cases, there was the possibility of prolongation of life had not this condition supervened. The development of endocarditis may be the decisive factor in bringing about the fatal issue.

DIFFERENTIAL DIAGNOSIS

It is clear from the foregoing that acute bacterial endocarditis may complicate any infectious disease in old people. It is to be considered as a diagnostic possibility in any febrile condition in the aged which is associated with bacteremia, and the more so if there is no response to specific therapy.

The differentiation from subacute bacterial endocarditis is important because, in our experience with the aged, the latter variety is twice as common as the acute, and, although it presents great diagnostic difficulties in old people, may more often be correctly diagnosed, because these patients are under observation for longer periods of time. Libman and Friedberg[21] have emphasized that, whereas in the acute form the primary lesion may overshadow the endocarditis, in the subacute type "the symptoms are due to the endocardial involvement or its complications. . . . The endocardial lesions produce symptoms by way of the associated toxemia and bacteremia, because of their effect on the valves and adjacent structures, and because the release of particles from the vegetations, usually containing bacteria, produces embolism and embolic aneurysms." As our series shows clearly, the course of the acute type is fulminating, and often diagnostically obscure by reason of the prostration of the patient, which tends to mask the symptoms. Commonly, the wealth of symptoms and signs makes it difficult to explain the clinical manifestations as a result of one disease. This is, of course, a frequent experience when dealing with aged patients, and has in part given point to the clinical aphorism: Disease in the aged is characterized by multiplicity, chronicity, and duplicity.

THERAPY

Medical opinion, until very recently, agreed that there was no treatment for acute bacterial endocarditis that offered even a moderate hope of success. The use of penicillin has not yet been sufficiently explored.[22] Its use in a case of acute hemolytic *Staphylococcus albus* endocarditis in a 23-year-old woman by one of us (F. D. Z.) produced only temporary improvement in the clinical picture, and during a short period the blood became sterile. At post-mortem examination there was no evidence that the pathologic process had been affected.

Two reports reveal results that are encouraging. The Alexanders[23] report the cure of an acute *Streptococcus hemolyticus* endocarditis in a man aged 62 years. The diagnosis was based on the changing character of the heart murmurs, the positive blood cultures, and the patient's septic temperature curve, in absence of other foci of infection. Sulfanilamide was given in doses of 15 grains (1 Gm.) every four hours for a period of six weeks.

Blumberg, Heine, and Lipshutz[24] report recovery from pneumococcus, Type XXVIII, endocarditis in the case of an 18-year-old man who was treated with sulfadiazine, sulfathiazole, and type-specific antipneumococcus serum. These authors have reviewed the literature and report two other cures of pneumococcus endocarditis.

These good results make it obligatory for physicians who are treating acute bacterial endocarditis in any age group to use sulfonamide drugs, penicillin, and specific antisera if possible. In addition, no reasonable surgical effort to eradicate or to drain the primary focus of infection should be omitted. In cases of superficial thrombophlebitis, ligation of the vein above the affected area is theoretically justified, but is of little value if a secondary focus on a heart valve has already been established.

Hamburger and his collaborators[25] have reported the case of a Negro woman, aged 43 years, "with an ultimately fatal Type VII pneumococcus endocarditis treated with sulfapyrazine intermittently over a period of six months. The pneumococci isolated at intervals during this treatment period showed progressive increase in sulfonamide resistance." They point out that this is a serious complication in the long-continued use of sulfonamides.

SUMMARY

In an effort to clarify the disease pictures encountered in the aged, nine cases of acute bacterial endocarditis, with autopsy, have been reported among patients whose ages ranged from 60 to 80 years. In none of these cases was the diagnosis made clinically. The bacteriologic, pathologic, and clinical features are discussed, and it is pointed out that the diagnosis is obscured by the multiplicity of symptoms and signs, as well as by the prostration of the patient. It is believed that these cases will be detected more often if the possibilty of this complication is borne in mind, especially when positive blood cultures are found in old people, and even in cases in which the diagnosis seems to be obvious. Clarification of the clinical problems posed by the aged patient offers many fascinating opportunities to the discerning physician.

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AURICULAR HEART SOUNDS IN AURICULAR FLUTTER

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SOON after the recognition of auricular flutter as a clinical entity, Cohn[1] stated that auricular sounds may occasionally be heard in this condition. Passing mention of auricular sounds in flutter has been made by others from time to time. The first graphic recording was that of Bennett and Kerr,[2] published in 1932. Four additional cases, complete with phonocardiograms, have been reported,[3-6] and one tracing has been published without any clinical information.[7, 8] Two other cases have been reported in which the fluttering auricle appeared to influence the intensity of the first ventricular sound.[9]

We have observed two cases of auricular flutter in which loud clicking sounds were associated with the flutter movement of the auricles. The sounds were transmitted to areas different from those hitherto described; their relation to the state of the myocardium and their position in the cardiac cycle were unusual. A discussion of our cases in relation to those observed by others, and of the probable factors responsible for auscultatory phenomena of this type appears justified. Table I summarizes the pertinent observations in the eight previous cases and in the two reported in this communication.

CASE REPORTS

CASE 1.—A 40-year-old riveter entered the hospital Jan. 17, 1944, complaining of shortness of breath and swelling of the ankles and abdomen for about three weeks. There was no history of previous heart disease or of rheumatic infection. Physical examination revealed a very obese, white man who was moderately dyspneic, cyanotic, and very edematous. The retinal arterioles were normal, and there was no evidence of hypertensive or arteriosclerotic retinopathy. The neck veins were markedly distended, but exhibited no pulsations. There were physical and roentgenologic signs of marked pulmonary congestion and edema. There was generalized cardiac enlargement, and the cardiothoracic ratio was 60 per cent. No murmurs were heard. The rhythm was regular, and the rate was constant at 150 beats per minute, suggesting auricular flutter or auricular paroxysmal tachycardia. The blood pressure was 110/70. Shifting dullness was noted in the abdomen, and no masses could be felt. Four plus edema was present in both lower extremities.

The patient was placed on a strict cardiac regimen consisting of rest in bed, oxygen, a salt-free diet, and large doses of digitalis. Abdominal paracentesis, ammonium chloride,

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and mercupurin were used to effect diuresis. Thiamine chloride was given in a dose of 60 mg. daily during the first week and 10 mg. daily thereafter because of the possibility of beriberi heart disease. However, no definite evidence was elicited to confirm the suspicion of beriberi.

On the seventh hospital day, after a total of 3.2 Gm. of digitalis leaf orally and 7 c.c. of cedilanid intravenously, the patient's general condition had improved somewhat, but signs of right ventricular failure were still present. The heart rate remained at 144 beats per minute, and could not be influenced by carotid sinus pressure. On the afternoon of the seventh day, and for the first time during his hospital stay, distinct, loud, and rapid clicking sounds were heard over the base, particularly in the second and third intercostal spaces at the left sternal border. Two of these sounds were heard during each cycle. With progressive digitalization, the ventricular rhythm became irregular and then regular, at a rate of about seventy beats per minute. At this time, the rate of the clicking sounds was approximately triple the ventricular rate. These extra sounds were heard consistently between the seventh and twentieth hospital days, except on the fourteenth day, when transient auricular fibrillation was present (confirmed by an electrocardiogram). The rhythm subsequently reverted to flutter and the extra sounds returned. The sounds varied in intensity and seemed particularly loud shortly after the intravenous injection of cedilanid. Between the seventh and twentieth hospital days, the patient lost a total of 55 pounds, and the heart became fully compensated. On the twentieth hospital day, after the patient had received a total of 7.7 Gm. of digitalis orally and 18 c.c. of cedilanid intravenously, normal sinus mechanism was re-established. The extra sounds over the base disappeared and did not return.

The patient was discharged Feg. 14, 1944, on a maintenance dose of digitalis, with the final diagnosis of paroxysmal auricular flutter with regular and irregular ventricular responses, cause unknown. A rheumatic valvular heart lesion was suspected, but could not be proved on clinical or roentgenologic examination.

Three weeks after the patient's discharge from the hospital, while changing a tire on his car, he was suddenly seized with extreme dyspnea, and died a few hours later. The heart was obtained after the body had been embalmed, and was examined by Dr. Bert Stofer. It revealed generalized enlargement, weighing 620 grams. The ratio of left to right ventricular weights was 1.5:1. This is within the normal range, and indicates that the left and right ventricles were proportionally hypertrophied.[11] The coronary arteries were patent throughout, and showed minimal sclerotic changes. There was no evidence of myocardial infarction. The endocardium and pericardium were normal. Sections of the ventricles and auricles were negative except for hypertrophy. Since no other tissues were examined, a pre-existent hypertension could not be excluded with certainty. The cause of the cardiac hypertrophy remained undetermined.

CASE 2.—A 36-year-old Negro housewife entered the hospital Sept. 1, 1943, with a history of repeated attacks of rheumatic fever since 1926, orthopnea and peripheral edema since April, 1943, and cough, fever, hemoptysis, and left-sided pleuritic pain of three days' duration. Physical examination revealed marked orthopnea, moderate cyanosis, slight jaundice, and 3 plus edema of the lower extremities. The blood pressure was 130/90. The jugular veins were markedly distended, and exhibited a strong, positive venous pulse. A large pleural effusion occupied the lower two-thirds of the left hemithorax. The apical impulse was barely palpable in the fifth intercostal space, 9 cm. to the left of the midline. The left border, by roentgenogram, was approximately 10.5 cm. to the left, and the right border was 9.5 cm. to the right, of the midline. The results of percussion and fluoroscopic examination were indicative of pericardial effusion. During the first week of hospitalization a loud pericardial friction rub was heard over the precordium to the left of the sternum, and a pleural rub was heard in the left axilla. In addition, there were endocardial murmurs which were identified after the disappearance of the rub as a to-and-fro basal murmur typical of aortic insufficiency. The rhythm was regular and the ventricular rate was consistently around 80 per minute. In the second and third intercostal spaces to the right of the sternum, a rapid, regular, slapping impulse could be distinctly felt at a rate approximately three times the ventricular rate. Corresponding with these palpable impulses, three loud clicking sounds were heard in each cycle, in addition to the to-and-fro blowing murmur of aortic insufficiency. These impulses and sounds were present throughout her hospital stay and were recorded graphically. A diagnosis was made of acute rheumatic pancarditis with 3:1 auricular flutter, complicating chronic rheumatic aortic and mitral valvulitis. The patient remained in the hospital for eighteen days and improved somewhat as a result of the administration of digitalis and diuretics. She refused thoracentesis and left the hospital against advice.

TABLE I. AURICULAR SOUNDS RECORDED IN AURICULAR FLUTTER*

NO.	AUTHORS	AGE	SEX	DIAGNOSIS	CARDIAC FAILURE	A-V RATIO	AURICULAR RATE	VENTRICULAR RATE	POSITION OF AURICULAR SOUND	TIME RELATION	REMARKS
1.	Bennett and Kerr, 1932[2]	-	-	-	-	Irregular ventricular response: 2:1, 3:1	270	102	Third intercostal space to left sternal border	Auricular sounds coincide with first and second ventricular sound and intensify the latter	The auricular sounds alternating in intensity following carotid sinus pressure; auricular electric alternans
2.	Cossio and Fongi,† 1936[7]	-	-	-	-	Complete A-V heart block	250	33	-	No systolic auricular sounds	-
2a.	Taquini‡[8]	-	-	-	-	Complete A-V heart block	220	33	-	Esophageal auricular sounds present in systole and diastole	Simultaneous sound-records from precordium and esophagus
3.	Routier, Mamou, and Lemant, 1936[9]	66	male	Atherosclerotic heart disease, Adams-Stokes seizures	Present	Complete A-V heart block	274	32	-	No auricular sounds, but change in intensity of first ventricular sound	
4.	Routier, Mamou, and Lemant, 1936[9]	52	male	Atherosclerotic heart disease, angina pectoris	Absent	Complete A-V heart block	?	36		As No. 3	

5.	Ludwig and Bener,§ 1936[3]	40	male	Syphilitic heart disease, aortic insufficiency, pericarditis	Present	Complete A-V heart block	250	40	Second and third intercostal spaces left sternal border	No systolic auricular sound	Auricular sounds disappear with compensation: *flutter gallop*. Autopsy revealed pericardiosternal adhesions
6.	Lian and Welti, 1938[4]	48	female	Hypertensive heart disease	Present	Complete A-V heart block	270?	45	Apex	No systolic auricular sound; reduplication of second ventricular sound	Auricular sounds disappear with compensation: *flutter gallop*
7.	Calo[5]	23	female	Rheumatic heart disease	Present	Irregular ventricular response: 3:1, 4:1	300	75	Entire precordium		Auricular sounds disappear with compensation: *flutter gallop*
8.	González Sabathié, Gaspary, and Voogd, 1942[6]	70	male	Hypertensive heart disease	Present	Complete A-V heart block	250	28	Midprecordial region	No systolic auricular sounds	
9.	Hecht and Myers, 1944	40	male	?	Present	Response: 2:1, 3:1, 4:1	259	65	Second intercostal space and along left sternal border	Auricular sounds late in systole and in diastole	Loudest during recovery from cardiac failure. Auricular sounds slightly irregular and influenced by cardiac systole
10.	Hecht and Myers, 1944	36	female	Rheumatic heart disease, pancarditis	Present	Response: 3:1	230	75	Second and third right intercostal spaces	Loudest auricular sound in systole	Auricular sounds slightly irregular and influenced by cardiac systole

*Two cases of auricular flutter have been reported by Laubry, Routier, and van Bogaert (Arch. d. mal. du coeur **25**: 321, 1935). From the observations presented it seems likely that auricular sounds were present, but no phonocardiographic tracings were made. Brief mention has occasionally been made of other cases, but since no clinical data or tracings are available, they have not been included in the present report. Reference made by a recent monograph[10] to auricular sounds in flutter reported by Roch, Sciclounoff, and Duchosal (Bull. et mém. Soc. méd. hôp. de Paris **50**: 1335, 1934) is erroneous because the sounds observed were caused by normal auricular complexes in complete A-V heart block in a patient suffering from attacks of 1:1 and 2:1 auricular flutter.

†Their tracing is reproduced in *The Heart Sounds in Normal and Pathological Conditions* by Orías and Braun-Menéndez,[10] p. 184, Fig. 91.

‡From the electrocardiogram it appears likely that this case is the same as that of Cossio and Fongi. Taquini's tracing, however, is obviously a different recording. No clinical data are available in either communication. The record of Taquini is included, for his observations on esophageal sounds are of considerable theoretical significance.

§Autopsy observations in this case are discussed by Ludwig.[11]

Six months later, after a period of almost complete rest in bed, a salt-poor diet, and digitalis medication at home, she was readmitted with a left-sided empyema which was drained surgically. Her cardiac condition had greatly improved. There was no trace of edema, very little dyspnea, and no orthopnea. The rhythm was completely regular, slow, and of sinus origin. The murmurs over the heart were similar to those observed before, suggesting a combined aortic and mitral valvulitis. The extra sounds and impulses formerly heard over the base of the heart had entirely disappeared.

Electrocardiograms.—Standard bipolar limb leads and standard unipolar precordial leads were recorded in both cases. In addition, unipolar limb leads (extremity potentials) and serial unipolar esophageal leads were obtained in the second case.

TABLE II. CASE 1. CYCLIC VARIATIONS OF THE AURICULAR SOUND (IN SECONDS)

AURICULAR SOUNDS				CORRESPONDING FLUTTER CYCLE (ECG)			
A	B	C	D	A	B	C	D
0.278	0.192	0.219	0.222	0.237	0.222	0.224	0.232
0.278	0.183	0.218	0.225	0.234	0.222	0.234	0.226
0.274			0.226	0.227			0.227
0.316	0.212	0.240	0.252	0.251	0.257	0.246	0.255
0.279	0.213	0.242	0.244	0.245	0.243	0.242	0.249
							0.248
0.276	0.180	0.199	0.224	0.225	0.219	0.234	0.227
0.282	0.187	0.211	0.225	0.225	0.224	0.223	0.226
	0.182	0.213	0.212		0.229	0.222	

A = Interval between systolic and first diastolic sound.
B = Interval between first diastolic and second diastolic sound.
C = Interval between second diastolic and first ventricular sound.
D = Interval between first ventricular and systolic auricular sound.
Note: Each group of figures represents measurements from one strip of film (enlarged photographs). Note the increase in time in *A* and the corresponding decrease in *B* in all instances of the sound measurements, without identical changes in the corresponding flutter cycle from the electrocardiogram.

The first record in Case 1, taken on the day of admission, revealed classical auricular flutter with a perfect 2:1 ventricular response (ventricular rate, 136, auricular rate, 272). The QRS complexes were upright in Leads I and II and of a vibratory type in Lead III. T waves were not discernible in the standard leads. Serial precordial leads (V_2, V_4, and V_6) were compatible with left ventricular enlargement. On the day the extra sounds were first noted a 2:1 response was present. On the following day the ratio had changed to 4:1 (auricular rate, 259, ventricular rate, 65). On the fourteenth hospital day, auricular fibrillation was recorded, with an irregular ventricular response. Left axis deviation was present (α = minus 18 degrees), and a U-shaped S-T depression was noted in standard bipolar limb leads and in precordial leads (digitalis medication). On the twentieth hospital day a record was obtained which for the first time revealed normal sinoauricular rhythm, with a heart rate of 79 beats per minute and a P-R interval of 0.24 second. The P waves were markedly split in Leads I and II, and biphasic in Lead V_1. The QRS and T waves appeared similar to those recorded on previous occasions. Late records taken on the twenty-fourth and on the twenty-ninth hospital days were similar except for the P-R interval, which gradually returned to normal values. Measurements of the rate of the flutter cycle taken from enlarged photographs and obtained with a Lucas comparator* revealed an average variation of the individual flutter cycles of 0.0065 second (0 to 0.0150 second) (Table II).

All records in Case 2 during the patient's first stay in the hospital revealed pure auricular flutter with a 3:1 ventricular response (auricular rate, 230, ven-

*Permission to use the comparator of the Heart Station of the University Hospital in Ann Arbor, Michigan, was given by Dr. F. N. Wilson, whose kindness is gratefully acknowledged.

tricular rate, 75). The QRS measured 0.07 second. Splintered initial ventricular complexes were present in Lead III. T waves could not be identified in any of the standard limb leads. Unipolar limb leads (extremity potentials) suggested a semivertically placed heart.[12] Unipolar leads taken over the second, third, and fourth intercostal space near the right sternal border and over the ensiform process (V_E) revealed small R waves and split S waves. A normal QRS pattern was present in standard precordial Leads V_2 to V_6. A U-shaped depression of the S-T segment, with inversion of T, was best seen in V_2, but occurred in other leads as well. These T-wave changes were thought to be caused in part by digitalis therapy. The flutter cycles were extremely constant, with an average variation of 0.009 second (0.002 to 0.022 second). When the patient returned several months later, normal sinus mechanism was present, with a heart rate of 88 beats per minute. The P-R interval measured 0.19 second. There was little change in the QRS and T waves. The P waves were unusually large and broad, particularly in Leads I and II. Standard precordial leads showed biphasic P waves in V_1, and serial unipolar esophageal leads from the auricular level showed P waves over twice the size of the corresponding QRS deflection. There was a late intrinsicoid auricular deflection. The auricular changes in standard bipolar and in serial unipolar leads were diagnostic of left auricular enlargement.[13] Unipolar extremity potentials suggested that the heart was more vertically placed than on previous examinations. On one occasion a transient A-V nodal rhythm was present.

Sound Records.—Sound records were obtained in the first case with the stethograph attached to the Cambridge Hospital model. A nonlogarithmic microphone was used. In the second case the sounds and impulses were registered with a Sanborn Tribeam electrocardiograph. A special chest piece was used, which allowed simultaneous registration of the sounds and of the mechanical impulses from the same area (linear and stethoscopic phonocardiograms). The chest piece was equipped with two outlets. One was connected to a crystal microphone of a logarithmic type for the recording of sounds, the other to a piezoelectric transducer for graphic registration of the mechanical vibrations of the chest wall. The arrangement has been described by Rappaport and Sprague.[14] Using a Lucas comparator, analyses of the time relations were made from the tracings and from enlarged photographs.

In the first case, it was noted that, when the microphone was placed over the area of maximal intensity of the abnormal sounds, six, instead of the usual two, heart sounds were present (Figs. 1 and 2). The first ventricular heart sound appeared to be markedly accentuated. The second sound seemed reduplicated, but close analysis revealed that the apparent splitting was due to an extra sound (*SAS*) which preceded the second ventricular sound by 0.055 second. This extra sound consisted of a few sharp vibrations of high frequency. Following the second sound at an interval of 0.13 second, a few low-pitched vibrations were noted; their character, frequency, and time relationship to the second sound suggested a protodiastolic gallop sound (*DG*). Two additional sounds were recorded in diastole (*DAS*), which not only were similar to one another in frequency, intensity, and duration, but also resembled closely the systolic extra sound (*SAS*) described above. If it is assumed that another extra sound coincided with the first ventricular sound and contributed to its unusual intensity, four extra sounds were present during each cycle: one buried in the first ventricular sound, one shortly preceding the second sound, one in early diastole, and one in mid-diastole. These four extra sounds corresponded with the four flutter waves of the simultaneously recorded electrocardiogram.

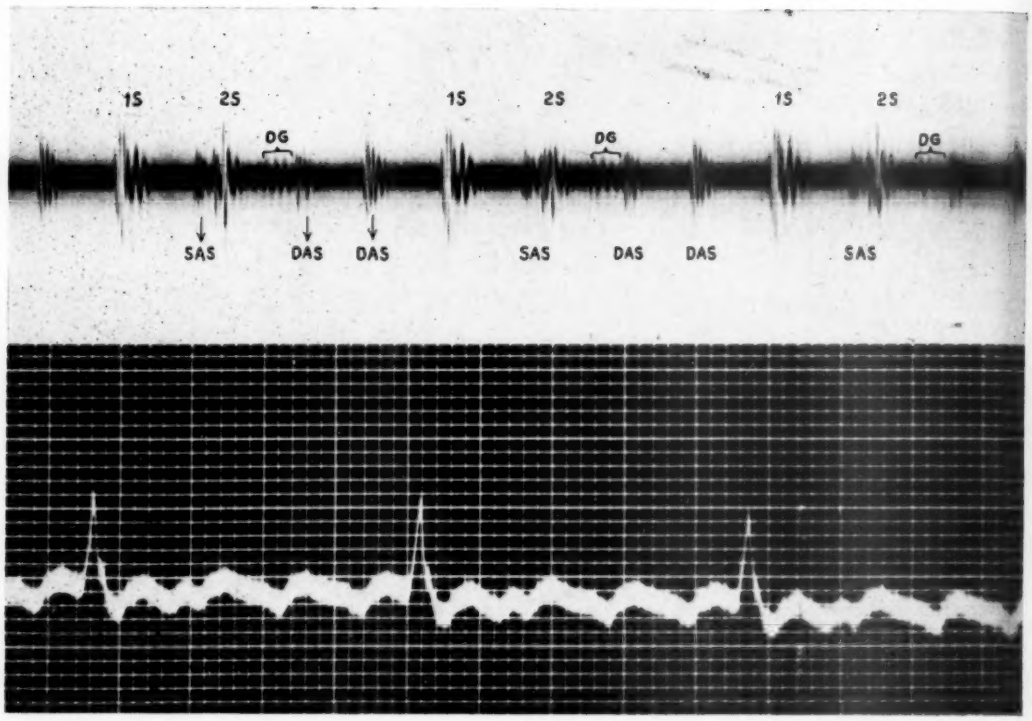

Fig. 1.—Case 1. Upper tracing: Sound records taken over second intercostal space, left sternal border. Lower tracing: Simultaneously recorded electrocardiogram. Lead II. *SAS* and *DAS*, auricular sounds; *1S* and *2S*, ventricular sounds; *DG*, protodiastolic gallop sound.

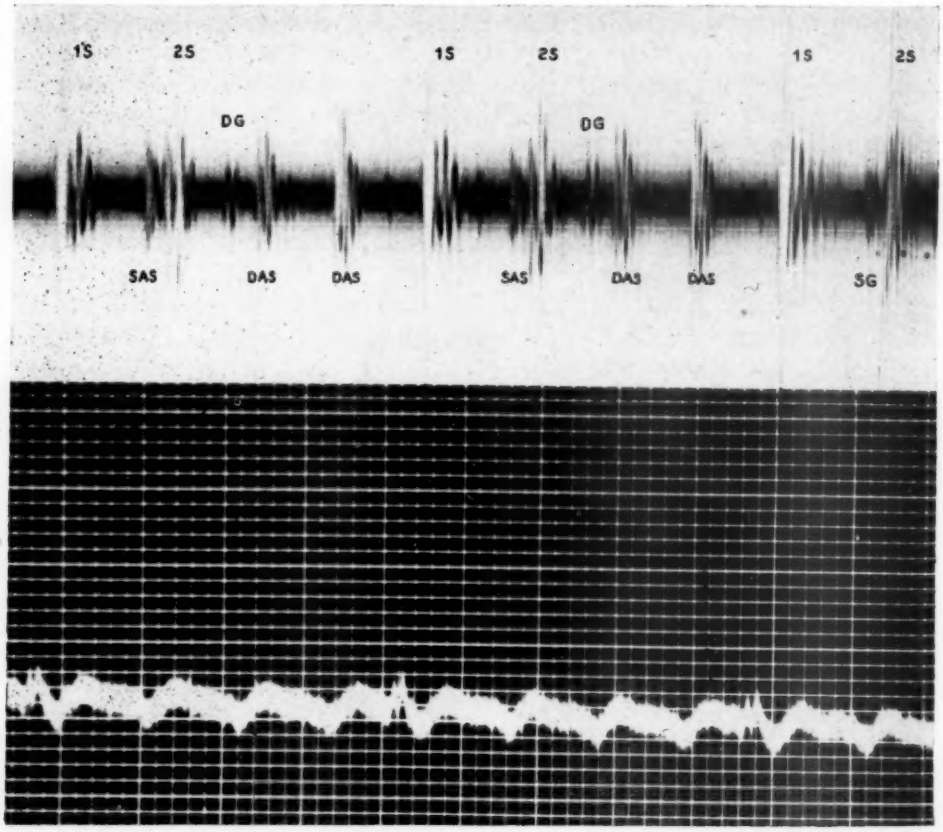

Fig. 2.—Case 1. Upper tracing: Sound records taken over second intercostal space, left sternal border. Lower tracing: Simultaneously recorded electrocardiogram, Lead III. *SAS* and *DAS*, auricular sounds; *1S* and *2S*, ventricular sounds; *DG*, protodiastolic gallop sound.

The diastolic extra sounds coincided with the trough of the flutter wave in the electrocardiogram. The trough also coincided with the first ventricular sound and immediately preceded the second ventricular sound. Assuming an extra sound superimposed upon the first ventricular sound, the four extra sounds would occur with regularity at about the same time in the flutter cycle of the electrocardiogram. They were almost equally spaced, and the assumption that these sounds were linked to the auricular contraction can hardly be questioned. With the establishment of normal sinus rhythm, the accentuation of the first ventricular sound, the extra sound in systole, and the two diastolic sounds were no longer present.

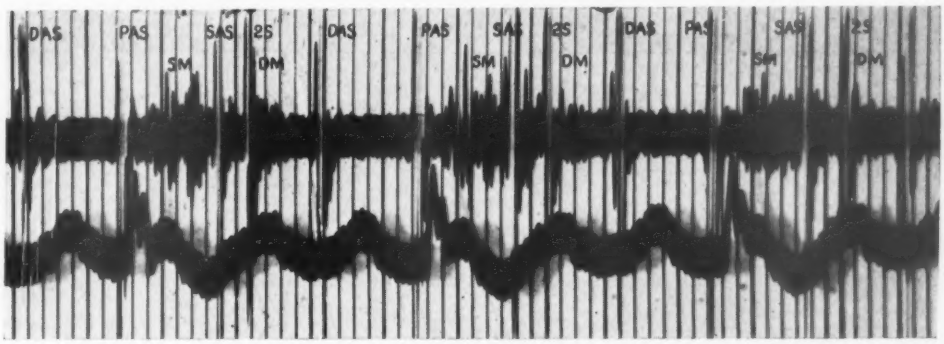

Fig. 3.—Case 2. Upper tracing: Sound records taken over second intercostal space, right sternal border. Lower tracing: Simultaneously recorded electrocardiogram, Lead III. *SAS*, *DAS*, and *PAS*, auricular sounds; *2S*, second ventricular sound (first sound buried in murmur *SM*); *SM—DM*, to-and-fro murmurs of aortic insufficiency. Note that there are five heart sounds and two murmurs per cycle.

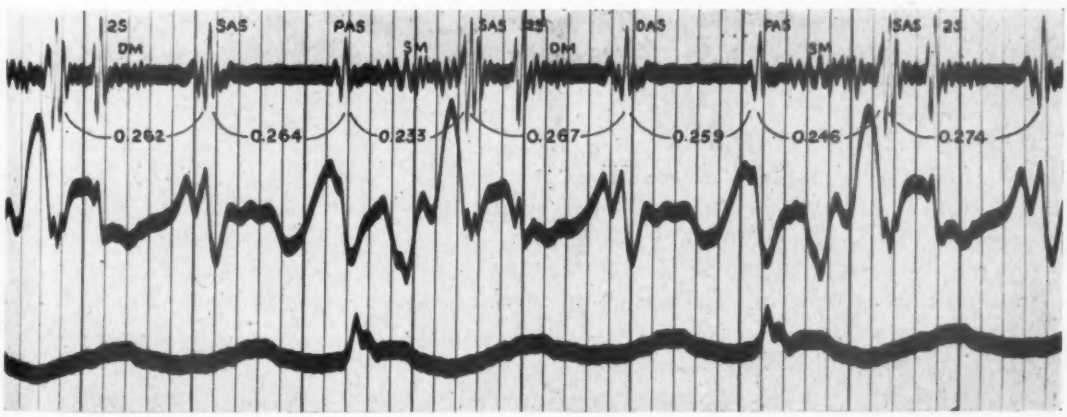

Fig. 4.—Case 2. Upper tracing: Sound records taken over second intercostal space, right sternal border. Middle tracing: Impulses over the same area. Lower tracing: Simultaneously recorded electrocardiogram, Lead III. *SAS*, *DAS*, *PAS*, auricular sounds, *2S*, second ventricular sound (first sound buried in murmur *SM*). *SM-DM*, to-and-fro murmur of aortic insufficiency. Intervals between auricular sounds in seconds.

Accurate measurements of the interval between the extra sounds revealed distinct differences which were apparently dependent on the state of ventricular contraction. The time between the systolic and the first diastolic extra sound was invariably longer than the time between the first and second diastolic sounds, or, in other words, the first diastolic extra sound appeared delayed. In contrast, the differences between the second diastolic and the first ventricular sound and between the first ventricular sound and the systolic extra sound were infinitesimal (Table II).

Phonocardiographic tracings in the second case were taken from the second and third intercostal spaces at the right sternal border, where the extra sounds

TABLE III. CASE 2. CYCLIC VARIATIONS OF THE AURICULAR SOUNDS (IN SECONDS)

AURICULAR SOUNDS			CORRESPONDING FLUTTER CYCLE (ECG)		
A	B	C	A	B	C
0.262	0.260	0.236	0.257	0.250	0.254
0.275	0.264	0.246	0.260	0.250	0.252
0.262	0.259	0.233			
0.272	0.254	0.232	0.262	0.254	0.244
0.276	0.263	0.244	0.260	0.253	0.263
0.262			0.260		
0.292	0.279	0.276	0.294	0.316	0.296
0.291	0.292	0.278	0.305	0.302	0.294
0.274	0.286	0.297	0.314	0.295	
0.276	0.246	0.233	0.252	0.257	0.246
0.264	0.246	0.251	0.258	0.254	0.245
	0.248				

A = Interval between systolic and first diastolic sound.
B = Interval between first diastolic and second diastolic sound.
C = Interval between second diastolic and systolic sound.

See note to Table II. Relatively little variation in cycle length is noted in the first and third group. Measurements on a number of other film strips were essentially similar to the one here represented.

appeared loudest, and were also obtained from several other points over the precordium. Over the first aortic auscultation point, a simultaneous recording was made of mechanical vibrations and sound effects with the electrocardiogram (Fig. 4). The analysis of the simultaneously recorded electrocardiograms and sound and pulse records was facilitated when the speed of the recording film was increased from the usual 25 to 75 mm. per second. It gave the following results:

The flutter waves of the electrocardiogram showed a fairly constant rate of 330 per minute. Occasionally slight slowing was demonstrable during systolic ventricular contraction (Table III), but accurate measurements were made difficult by the continuous movement of the string and the absence of sharp end points.

Five mechanical vibrations were recorded. Two apparently coincided with the first and second ventricular sound and were of lower voltage than the remaining three, which appeared evenly spaced, one in systole (following the QRS complex by 0.4 second), and two in diastole. Again there was a slight increase in the interval between the systolic and the first diastolic thrust, and a corresponding decrease in time between the first and second diastolic beat.

Sound records over the same area (second and third right intercostal space at right sternal border) (Figs. 3 and 4) showed a loud, low-pitched systolic murmur (*SM*). In some of the records, particularly when the two-outlet chest piece was employed (Fig. 4), the murmur tended to obscure the first ventricular sound (filter effect). Late in systole a loud snapping sound was present, usually the loudest sound of the cycle (*SAS*). This sound was followed by the second ventricular sound (*2S*) by about 0.08 second. The second sound led into a short, relatively high-pitched, decrescendo type of diastolic murmur (*DM*). Two extra sounds were noted in diastole. One of them appeared in early diastole (*DAS*) and was usually somewhat less intense than either the systolic extra sound or the second ventricular sound. The second diastolic extra sound appeared in presystole (*PAS*) and was usually fainter than any of the other sounds recorded. The three extra sounds, two in diastole and one in systole, were much alike. They were of short duration, rarely exceeding 0.04 second. With the technique employed, they showed not more than about three to four rapid oscillations of relatively high amplitude, which was strikingly different from the pattern usually noted in "normal" auricular sounds or au-

ricular sounds observed in atrioventricular block. Again the three sounds were not spaced evenly: the first diastolic sound appeared to be delayed in some, but not in all, of the records obtained (Table III).

The mechanical impulses recorded seemed to precede the sounds by a fraction of a second (Fig. 4). Both sounds and impulses occurred during the dale of the flutter wave in a simultaneously recorded Lead III. The over-all frequency of these extra sounds and its mechanical corollary coincided very closely with that of the fluttering auricle, for the delay of the first diastolic sound was made up by a slight shortening of the interval from the first to the second diastolic sound (Fig. 4, Table III). The sounds disappeared after normal sinus rhythm had been re-established. It seems certain that the extra sounds and impulses recorded were closely related to the flutter movement of the auricles.

DISCUSSION

Electrophysiologically, auricular flutter and auricular fibrillation have a fundamentally similar mechanism. In both, a continuous wave of excitation travels in a strip of muscle around one or two of the large venous openings (mother wave) and gives rise to tangential offshoots which reach the A-V node at regular or irregular intervals. Minor differences in the speed and pathway of the excitation wave and in the responsiveness of auricular muscle determine whether auricular fibrillation or flutter is present. Mechanically, the differences between auricular flutter and auricular fibrillation are pronounced and fundamental. Auricular fibrillation consists of incoordinate tremulations of auricular muscle which are incapable of properly filling the ventricular cavities at any time. Auricular flutter consists of rapid but rhythmic and coordinate contraction of auricular muscle, as has been demonstrated clinically by careful fluoroscopic examination with or without the aid of barium in the esophagus.[15, 16] Coordinate contractions in auricular flutter have also been demonstrated by the roentgenkymograph.[17]

Thus, conditions for the production of sounds from the auricles, namely, muscular contraction and propulsion of blood, are present in auricular flutter but are absent in auricular fibrillation. Auricular sounds have never been observed, and are inconceivable, in auricular fibrillation. There seems to be no doubt that the fluttering auricle was in some way responsible for the extra sounds recorded in our two cases, as well as in the others summarized in Table I.

The extreme rarity of audible auricular sounds in flutter is not unexpected when the incidence of audible auricular sounds in normal hearts beating in sinus rhythm is taken into consideration. The sound of the normal auricular contraction is so low in intensity and pitch and so near the first ventricular sound that it is ordinarily inaudible. Even when the auricular and ventricular contractions are widely separated by a conduction defect, the auricular sounds are not easily heard. The prolonged diastolic silence in auriculoventricular block apparently facilitates detection of sounds from the fluttering, as well as from the normally contracting, auricle. Four of the patients in Table I had auricular flutter and complete auriculoventricular block, a rare combination of cardiac irregularities.[18, 19] Auricular sounds, with sinus mechanism, which are below the threshold of the human ear are frequently recordable by phonocardiogram ("subsonic" auricular sounds). It is possible that routine phonocardiograms in cases of auricular flutter would reveal that auricular sounds are more common than has hitherto been supposed.

The cases of Routier, Mamou, and Lemant[9] had atrioventricular heart block and auricular flutter, but no direct auricular sounds. The rhythmic

activity of the auricles became apparent by a change in the intensity of the first ventricular sound, which appeared loudest when the crest of the flutter wave preceded the onset of QRS by about 0.08 to 0.12 second. One is inclined to assume that the change in intensity of the first ventricular sound in their cases was at least in part caused by the influence of auricular contraction on the wave of ventricular filling and on the position of the atrioventricular valves.

Auscultatory phenomena directly or indirectly related to the auricle tend to become intensified in the failing heart, and may be manifested by gallop rhythm over the ventricle; this is customarily explained by the inrush of blood pounding against the ventricular walls.[10]

In three of the cases included in Table I, the extra sounds were heard during heart failure and disappeared with compensation, despite the presence of flutter. In two of these cases, the extra sounds were best heard at the apex, suggesting a ventricular origin. The location of the sounds in these cases and the apparent relation to the functional state of the heart muscle justified the term "flutter gallop" in instances of this kind. This phenomenon could not account for the extra sounds in our cases for the following reasons: (1) The sounds were picked up at the base rather than at the apex; (2) One of the sounds occurred during ventricular systole at a time when the atrioventricular valves were closed.

Our cases are the only ones on record in which auricular sounds of the fluttering auricle could be registered from the precordium during ventricular systole. Loud auricular sounds beginning before, but ending during, the earlier part of ventricular systole have been recorded through a microphone placed in the esophagus.[8, 20, 21] Using such a microphone, systolic auricular sounds have been observed in cases of atrioventricular dissociation,[8] and Taquini has published an esophageal phonocardiogram in a case of auricular flutter in which sounds synchronous with the flutter waves were present in ventricular systole as well as during diastole. Although it has been accepted that sounds caused by muscular contraction of the auricles can be recorded from the esophagus, many investigators contend that such sounds cannot be registered from the precordium, and have assumed that precordial sounds associated with auricular activity are not produced in the auricles, but are set up secondarily in the atrioventricular valves or in the ventricles.[7, 8, 10, 22-27] The fact that, in both of our cases, loud sounds synchronous with auricular activity were recorded over the base during ventricular systole is against the foregoing hypothesis.

The extra sounds in our two cases differed in several respects from the sounds reported in the other eight cases of flutter, as well as from the auricular sounds in normal sinus rhythm. Sounds directly or indirectly resulting from auricular contraction are usually heard best over the midprecordium or at the apex (i.e., in the direction of blood flow), rather than at the pulmonary or aortic auscultation points, as in our cases. The usual auricular sounds are much less intense and differ strikingly in pitch and quality from the clicking sounds present in our cases. These differences are also apparent in the phonocardiographic records.

In view of the known pericarditis in Case 2, an auricular friction rub was considered. However, the auscultatory and phonocardiographic characteristics of the sounds in these cases differed markedly from the auricular friction rub described by others.[28]

The coincidence of the extra sounds in our cases with the trough of the flutter waves in the electrocardiogram indicates that they were related in some

way to the flutter movement of the auricles. The ability to palpate and graphically record an impulse coincident with the extra sounds and flutter wave in Case 2 would suggest that the contractions of the fluttering auricles were exceptionally strong, perhaps sufficient to account for the unusual quality and intensity of the sounds. The location of the sounds and impulses in the second intercostal space on the right may have been due to cardiac displacement or to transmission from the right auricle into the superior vena cava. The fact that the extra sounds in Case 1 became distinctly louder shortly after the intravenous injection of cedilanid also suggests a possible relationship between the strength of the muscular contraction and the intensity of the sounds. However, this explanation does not account for the delayed appearance of the auricular sound located in early diastole. The interval between the auricular sound which fell during ventricular systole and the next auricular sound in protodiastole was often, although not always, distinctly longer than the intervals between any other pair of auricular sounds. This was observed in both cases and has not been noted before.

The postsystolic delay, together with the clicking quality and unusual loudness of the sounds associated with the flutter movement, raises the question whether they were extracardiac in origin, i.e., possibly caused by adhesions drawn taut by the flutter contractions. The apparent forcefulness of the auricular beats in both cases would also support this explanation, as does their increase in intensity following the intravenous administration of digitalis. "Systolic ventricular clicks" are aggravated by increasing the force of ventricular contraction.[29] The delay in the sound which followed ventricular systole might be explained by the change in position of the heart associated with ventricular contraction. The character of the sounds resembled the "systolic ventricular click" which has been reported in association with pleuropericardial adhesions.[29-32] Assuming an "auricular click" as the cause of the sounds observed, it should be noted that pleurisy and pericarditis were present in Case 2 at the time the auricular sounds were heard. Extensive pericardial adhesions were found at autopsy in one of the cases of auricular flutter with audible auricular sounds.[17] However, no evidence of active or adhesive pericarditis was found in Case 1.

SUMMARY

1. Two cases of auricular flutter in which audible auricular sounds were graphically recorded are added to the eight cases already reported.

2. The cases presented were unusual in the following respects:

a. The exceptional loudness of the auricular sounds, which approached or exceeded the ventricular sounds in intensity,

b. The point of maximal intensity in the pulmonic and aortic auscultation points, respectively,

c. The presence of palpable and mechanically recordable impulses synchronous with the auricular sounds and the flutter waves in one case,

d. The intensification of the sounds by the intravenous injection of a digitalis glycoside in the other case,

e. Perfect synchrony with the flutter wave of the electrocardiogram except in the cycle immediately following ventricular systole, where there was a slight but significant delay in the appearance of the sound,

f. The clicking character of the sounds,

g. The occurrence of a loud auricular sound during ventricular systole.

3. Two alternate explanations are offered for the sounds observed: The flutter contractions of the auricles may have been audible because of their unusual forcefulness, or an "auricular click" associated with pleuropericardial adhesions may have been present.

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ACUTE BENIGN PERICARDITIS

A Report of Two Cases in Young Adults

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Succasunna, N. J.

THE frequency with which fatal heart disease has been found in young adults at autopsy makes it imperative that continued efforts be directed toward the early recognition of cardiovascular disease that may be of a benign nature. This is particularly true in this period of universal war, when both the civilian and soldier are being subjected to unusual and prolonged physical strain. Pericardial irritation has long been recognized as of frequent occurrence in rheumatic fever, the earlier stages of acute coronary occlusion, cardiac trauma, and, less frequently, in tuberculosis. Relatively few cases have been reported in which the only preceding incident was a common cold.

Barnes and Burchell[1] recently reported fourteen cases of acute pericarditis of benign, nonsuppurative nature; serial electrocardiographic studies differentiated the condition from acute coronary occlusion. Katz, et al.,[2] and Scott, et al.,[3] in 1929, introduced both experimental and clinical evidence in support of the diagnosis of acute pericarditis by means of the electrocardiogram in animals and man, respectively. Wiggers,[4] in 1930, experimenting with surface application of potassium salts to the pericardium of animals, obtained electrocardiographic changes closely resembling those later noted in cases of proved pericarditis. The largest group of cases (fifty-seven) was reported by Bellet and McMillan,[5] in 1938.

Two additional cases with complete clinical recovery are being reported because of their occurrence in young people, the initial resemblance to acute coronary occlusion, and the changes found in standard and multiple precordial lead electrocardiograms and the orthodiagram.

CASE REPORTS

Case 1.—W. B., a white male powder worker, aged 24 years, gave a history of severe clamping precordial pain of twelve hours' duration, gradual in onset and progressive in severity. When first seen he was pale, with a cyanotic hue to the lips and nail beds, and was dyspneic, orthopneic, and weak, but not perspiring.

The patient stated he had had a slight cold a week previously, but had continued to work. There was no past history of cardiovascular disease in this man or his family. For eight months he had had a recurrent discharge from one of his ears following traumatic rupture of the eardrum.

Physical examination revealed a definite friction rub, best heard in the second and third left intercostal spaces close to the sternum. The heart sounds were of poor quality, with no murmurs or arrhythmias. The lungs were normal throughout. There was slight tenderness in the epigastrium. The liver was not palpable, and the abdomen was otherwise normal. The extremities were not edematous. There was no evidence of peripheral vascular disease. The blood pressure was 120/80.

Further examination by means of the orthodiagram showed slight generalized cardiac enlargement (Fig. 1).

Twenty hours after the acute onset his temperature was 102° F., his pulse rate, 96, and regular, and his blood pressure, 120/80. The friction rub was more pronounced. The following day the temperature was 99.8° F., the pulse rate, 94, the rhythm, regular, and the blood pressure, 100/80. The friction rub had disappeared. The leucocyte count was

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6,720 per cubic millimeter with 53 per cent polymorphonuclears, 40 per cent lymphocytes, 3 per cent monocytes, 2 per cent eosinophiles, 1 per cent band forms, and 1 per cent Türk's cells. The hemoglobin was 114 per cent (Sahli). An erythrocyte count was not done.

On the third day of the illness the blood pressure was 114/72. The temperature was 98.6° F., and it remained normal thereafter. On the seventh day of the illness, the sedimentation rate of the erythrocytes was 20 mm. in one hour (Westergren).

An orthodiagram (Fig. 2) fifteen days after the patient was first seen showed a smaller transverse diameter of the heart, with a more nearly straightened left border.

The patient returned to work three weeks after the onset of this attack. He has had no recurrence of discomfort, and his functional capacity has not been impaired.

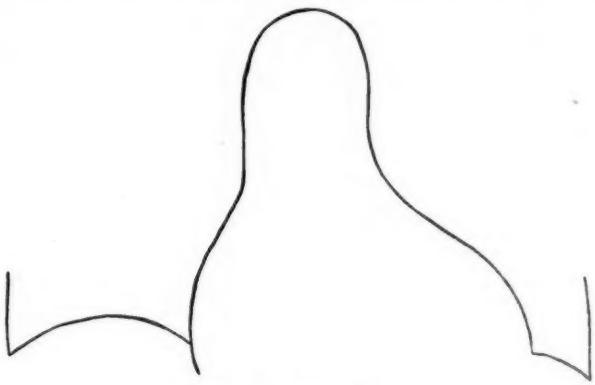

Fig. 1.—Case 1. Description in text.

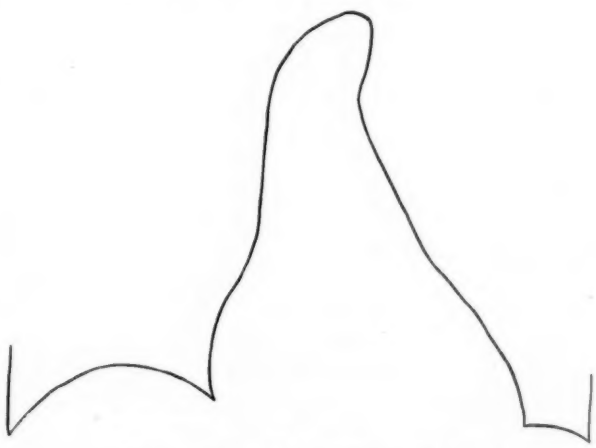

Fig. 2.—Case 1. Description in text.

As will be noted in the series of electrocardiograms (Fig. 3), there was a change from the first apparently normal tracing (T_3 negative) to partial flattening of the T waves in the standard leads, slight inversion of the T wave in precordial Leads $CF_{1, 2, 3 \text{ and } 4}$, and flattening of T in CF_5 two days later. The partial flattening and inversion of the T waves disappeared on the sixth day except in the precordial leads, where the flattening persisted.

The electrocardiogram appeared to be consistent with a diagnosis of pericardial irritation, even though the RS-T segments were not significantly elevated. No abnormal Q waves were present, and there was no reciprocal depression of the S-T segment which is frequently noted in coronary occlusion. Had further studies been made, it is possible that more inversion of the T waves in Leads I and II might have been found.

The changes in the configuration of the heart shadow, as shown by the orthodiagram, offered additional confirmatory evidence.

CASE 2.—G. E., a white male truck driver, aged 30 years, gave a history of pain in the midanterior chest, radiating in all directions, and later to the medial surface of the left

upper arm to the elbow as an ache. This occurred while driving a truck at night, 300 miles from his home. The pain was accentuated by respiration and movement. He felt weak and perspired. He stopped the truck and slept two hours, during which time the pain subsided, and then he drove home. The pain recurred fourteen hours later and became progressively worse overnight.

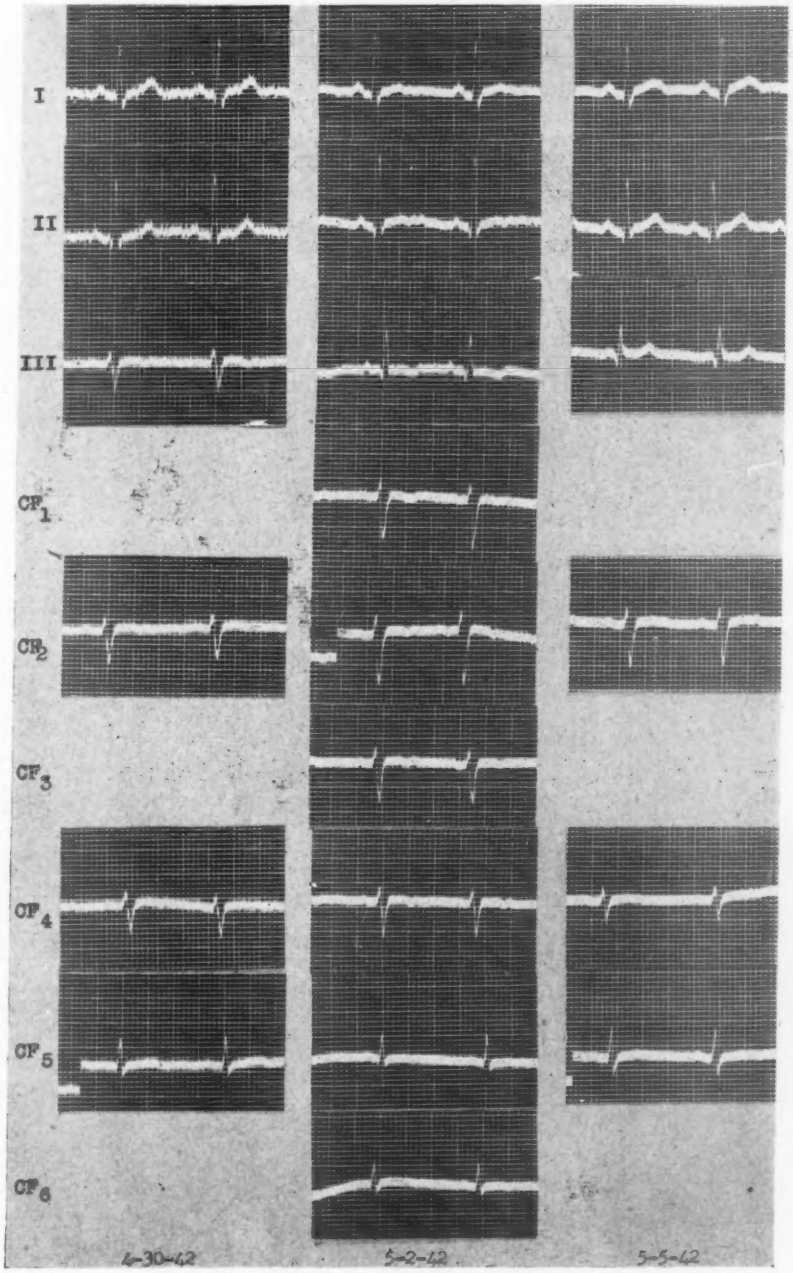

Fig. 3.—Case 1. Description in text.

There was a history of slight nasopharyngitis a week previously. The patient's and his family history were negative for cardiovascular disease.

On physical examination, thirty-three hours after the onset, the patient was orthopneic, pale, and apprehensive. There was a short presystolic scratching friction rub in the lower sternal region. There were no murmurs or arrhythmias, and there was no evidence of cardiac enlargement on percussion. The lungs, abdomen, and extremities were normal.

There were no signs of peripheral vascular disease. The temperature was 98° F., the pulse rate, 80, and the respirations, 36. The blood pressure was 136/78. The sedimentation rate of the erythrocytes was 3 mm. in one hour (Westergren). The leucocyte count was 10,480 per cubic millimeter, with 80 per cent polymorphonuclears, 10 per cent lymphocytes, 4 per cent monocytes, and 6 per cent basophiles. The hemoglobin was 104 per cent (Sahli). The erythrocyte count was 4,790,000 per cubic millimeter.

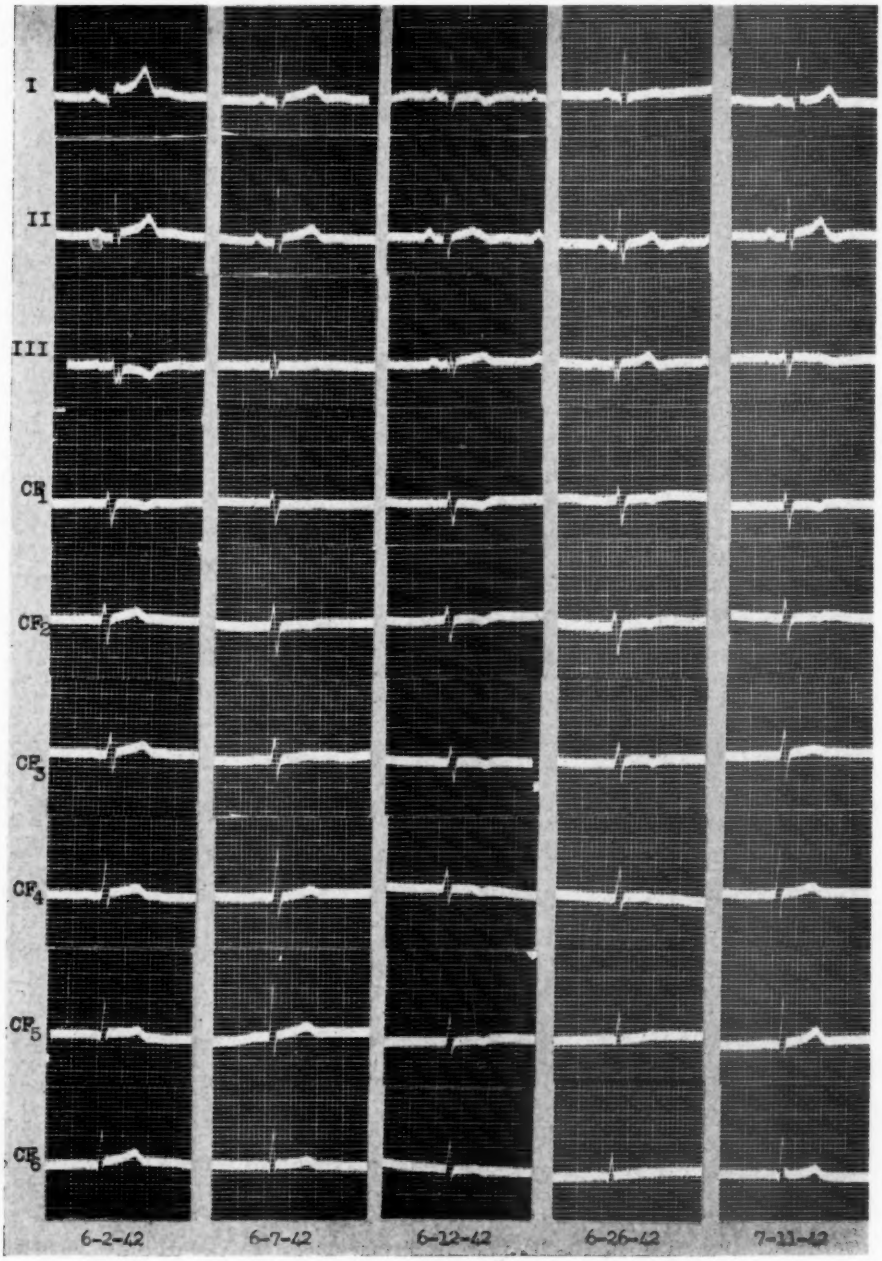

Fig. 4.—Case 2. Description in text.

On the following day the oral temperature was 100° F., the pulse rate, 80, and regular, and the respirations 30. The friction sound was more pronounced, orthopnea was still present, and the pain was described as a soreness in the precordium. On the fourth day his temperature, pulse rate, and respirations were normal; the blood pressure was 110/60, and both the friction rub and pain had subsided. By the eleventh day of the illness the

leucocyte count had dropped to 6,760 per cubic millimeter, with 59 per cent polymorphonuclears, 38 per cent lymphocytes, and 3 per cent monocytes. The erythrocyte count was practically unchanged.

Fluoroscopic examination three and one-half weeks after the onset revealed no evidence of pericardial fluid or cardiac enlargement. The patient returned to work, and there has been no recurrence of symptoms.

The electrocardiograms in this case more strikingly correspond to the accepted pattern of acute pericarditis (Fig. 4). Note the early elevation of RS-$T_{1 \text{ and } 2}$ and the inversion of T_3, with the normal precordial series, then the return of RS-T to normal, and the gradual inversion of the T waves in all other leads (except in Lead II, where it became somewhat dome-shaped). These changes appeared first in Lead I and the precordial leads and subsequently disappeared. T_3 changed from negative to positive and then returned to negative. There were no abnormal Q waves and no reciprocal depression of the S-T segment.

SUMMARY

Two cases of acute benign pericarditis of unknown cause are reported, with multiple lead electrocardiographic changes in both, and significant changes in the orthodiagram in one. Both cases occurred in young adults without previous cardiovascular disease. In each case there was a history of a recent upper respiratory infection. The onset in each was suggestive of acute coronary occlusion. The period of disability in Case 1 was twenty-one days, and, in Case 2, twenty-eight days. Both patients returned to full duty. No recurrence of symptoms has been noted to date.

In Case 1 an electrocardiogram eight and one-half months after the acute attack was normal.

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ELECTROCARDIOGRAPHIC CHANGES IN ACTIVE DUODENAL AND GALL BLADDER DISEASE

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A GROWING literature attests the relationship between upper right abdominal disease and attacks of acute substernal pain which simulate angina pectoris or even coronary occlusion. The subject has been presented recently by Miller[1] and Levy and Boas.[2] An accurate differential diagnosis is essential, especially when surgical risk is involved.

The pain of coronary occlusion is sometimes referred to the abdomen and resembles that of acute upper abdominal disease. In such instances we rely heavily on the electrocardiogram in the differential diagnosis. Our aging population has produced a higher incidence of associated gall bladder and coronary disease, and, rarely, acute conditions in both occur simultaneously.

The following records are of patients who had active gall bladder or duodenal disease; their acute attacks of pain were referred to the substernal region and resembled angina pectoris or coronary occlusion. This type of patient presents a serious problem, and emphasizes the importance of the gastrointestinal tract in cardiology. It is important that the electrocardiographic changes which are found in the presence of these diseases be not misinterpreted. The electrocardiograms of these patients showed an unusual alteration which may be important in the differential diagnosis of acute duodenal or gall bladder disease and coronary occlusion.

CASE REPORTS

CASE 1.—*History.*—This 44-year-old man had experienced vague abdominal distress for many weeks, and had taken soda to relieve upper abdominal and lower chest pressure. His acute illness occurred in April, 1940. While removing his car from the garage after breakfast, he was seized with severe burning pain beneath his sternum which did not radiate, was made worse by movement, and lasted five minutes. He continued with his usual activities during the following few weeks, and had several similar but less severe substernal pains after exertion which were relieved by rest. While performing strenuous activity he had a more severe attack of substernal pain which was accompanied by sweating, mild nausea, and prostration. This attack required morphine, and, during the following night, he was awakened by a most severe attack of substernal pain, with nausea, vomiting, sweating, and the appearance of shock, which again required morphine for relief.

Examination.—He was seen ten hours after his last severe attack of pain, when he was free of symptoms. His pulse rate was 72, and his blood pressure, 100/60. The pupillary and tendon reflexes were normal, and nothing unusual was noted in the lungs. Examination of the heart and blood vessels was negative. Slight, deep, epigastric tenderness was noted. Fluoroscopic examination of the chest a few days later showed nothing abnormal about the lungs or diaphragm, and the heart and aorta were of normal size and shape.

Electrocardiogram.—Fig. 1, *A*, taken May 10, 1940, the day after his most severe attack of substernal pain, shows normal limb leads, but CR_4 shows an isoelectric R-T segment and a positive-negative T wave, the inverted portion being deep and pointed. Fig. 1, *B*, taken June 10, 1940, just prior to ulcer therapy, but after four weeks of rest in bed, shows the same, but less marked, changes in the T waves of Lead CR_4. Fig. 1, *C*, was taken July 2, 1940, after three weeks of treatment for the duodenal ulcer, and is normal in all four leads. Fig. 1, *D*, was taken Nov. 3, 1943. The standard limb leads and chest Leads $CR_{1, 2 \text{ and } 5}$ are normal.

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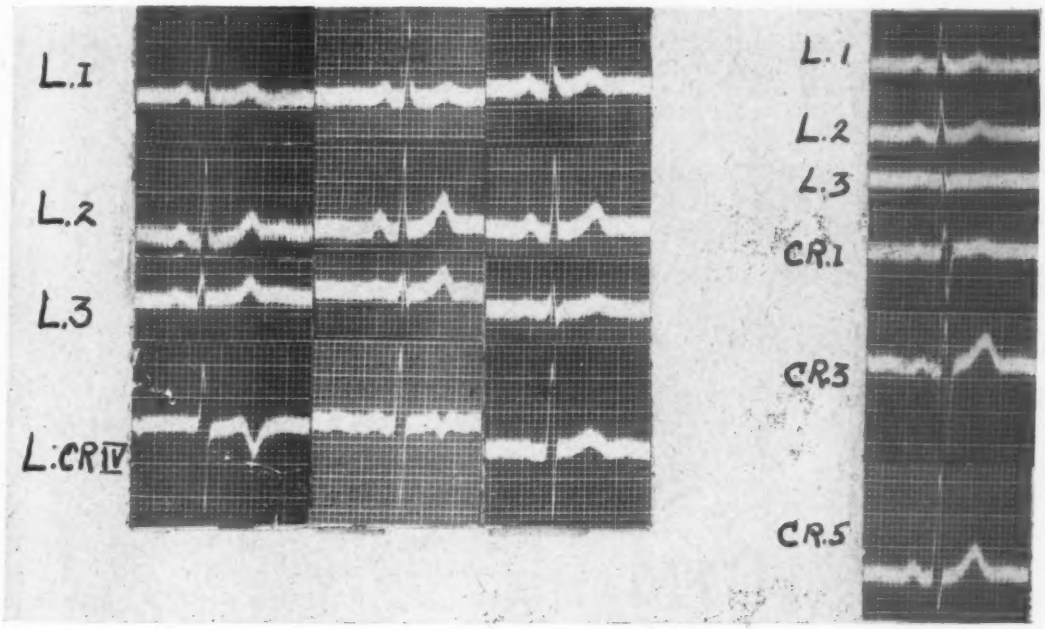
Treatment and Progress.—He was hospitalized in May, 1940, after his last severe attack of substernal pain, and a few weeks later a gastrointestinal roentgenologic examination revealed: "Chronic duodenal ulcer, with associated irritability and spasm suggesting activity at this time." He was placed on ulcer therapy June 11, 1940. On July 2, 1940, he was free from all symptoms, but in December, 1940, he noted a slight burning pain in the lower part of the right hemithorax, radiating up to the substernal region, which occurred following exertion after meals. On Nov. 3, 1943, he was free of symptoms. He had been working very hard since December, 1940, without dietary restrictions, and there had been no recurrence of the chest pains or any other symptoms. The upper gastrointestinal roentgenologic examination, made Nov. 4, 1943, showed "slight deformity of duodenal bulb, but no evidence of activity."



A. *B.* *C.* *D.*

Fig. 1.—Diagnosis: acute duodenal ulcer. *A* was taken May 10, 1940, after an acute attack of chest pain; the limb leads are normal, and the T wave in CR_4 is plus-minus diphasic. *B*, was taken June 10, 1940, just prior to starting ulcer therapy, but, after four weeks of rest in bed, the diphasic T wave in Lead CR_4 was less pronounced. *C* was taken July 2, 1940, after three weeks of ulcer therapy, and all leads are normal. *D*, taken Nov. 3, 1943, includes chest Leads $C_{1-3 \text{ and } 5}$, and is entirely normal.

CASE 2.—*History.*—This 47-year-old man had had "stomach trouble" for thirty years. Eating certain foods would cause flatulence, hyperacidity, and vague abdominal distress. A gastrointestinal roentgenologic examination, done in 1936, showed "mild spasm of the pylorus, with a few retained flecks of barium in the first portion of the duodenum, but no filling defect." Appendectomy was performed at that time, and his abdominal symptoms were relieved until March, 1940. During a long walk he suddenly had severe pain which was squeezing in the precordial and lower sternal regions and radiated into the left arm. Standing still gave some relief, and he was able to continue on to his home. On the following days he had similar pains which were less severe. While at rest in bed he had a very severe attack of pain in the chest which radiated into both arms, and the left arm continued to ache for several hours. There was no nausea or vomiting, but he sweat profusely and was dyspneic. The succeeding night he was awakened by a similar severe pain which spread over the entire anterior portion of the chest.

Examination.—He was seen a few days after his last severe attack of pain, when he was free of symptoms. His resting pulse rate was 72, and his blood pressure was 130/90. The pupillary and tendon reflexes were normal, and examination of the fundi was negative. Both lungs were normal, and the heart was of normal size; its rhythm was regular, and the sounds were good, with no murmurs and normal accentuations at the base. There was slight tenderness deep in the epigastrium, but no muscle spasm, and there were no palpable

abdominal masses or viscera. The extremities were negative. Fluoroscopic examination of the chest revealed normal heart and aortic shadows and clear lungs.

Electrocardiogram.—An electrocardiogram had been taken in 1934 and reported as normal. Fig. 2, *A*, was taken at his initial examination on April 29, 1940, and shows a flattened T_1, with slight plus-minus inversion; CR_4 has a normal R wave, the R-T segment is isoelectric, and there is a positive-negative T wave, with the inverted portion sharply pointed. Fig. 2, *B*, was taken May 7, 1940, and shows normal limb leads and the changes previously noted still present in CR_4, but with lower T-wave amplitude. On April 29, 1941, Fig. 2, *C*, was taken and is normal; the T wave in CR_4 is now entirely upright and of normal contour and amplitude. His latest curve, Fig. 2, *D*, taken Feb. 3, 1944, includes chest leads CR_{1-6} and is normal.

Treatment and Progress.—He was in the hospital during May, 1940. The gastrointestinal roentgenologic examination revealed "diverticulum of the duodenum, with signs of irritability." After several weeks of rest and dietary and medical treatment, the symptoms disappeared except for slight distress in the lower sternal region on exertion. On Feb. 3, 1944, he was free of all symptoms and was carrying on his regular work, but he was still following dietary restrictions.

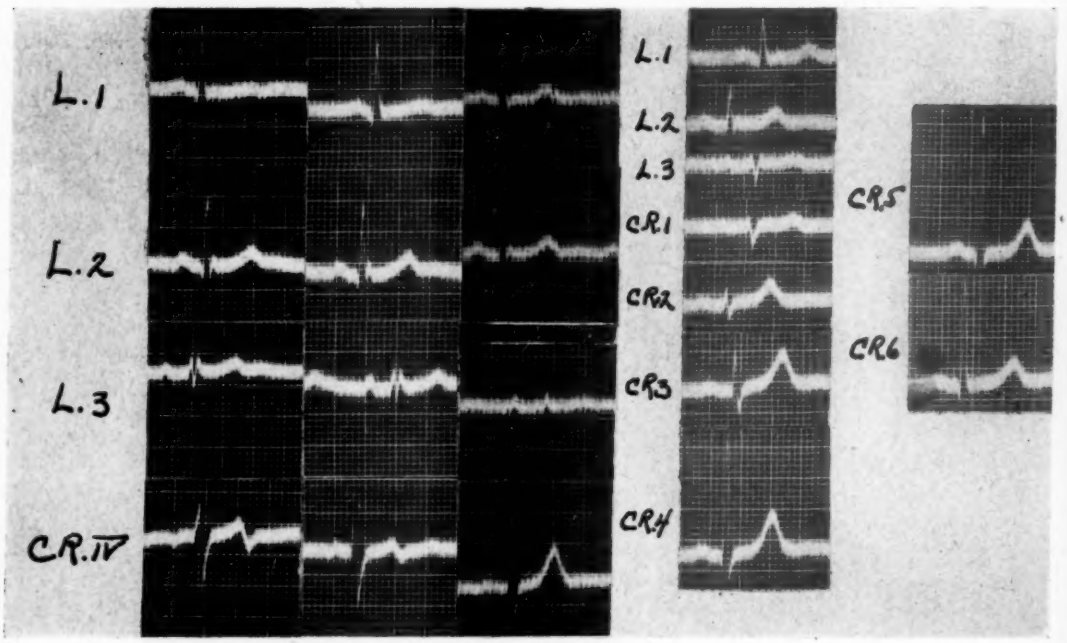
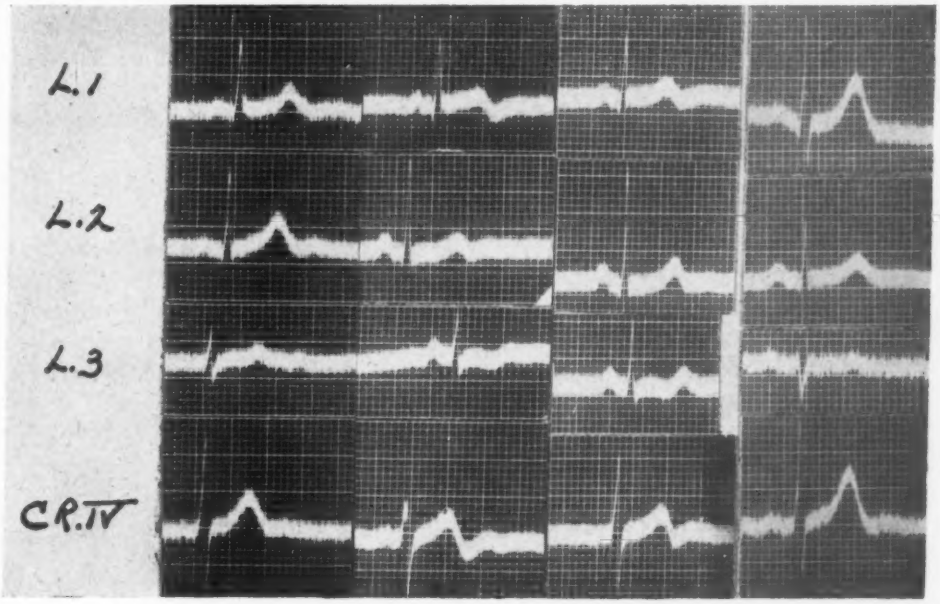


Fig. 2.—Diagnosis: acute duodenal diverticulitis. *A*, taken April 29, 1940, twenty-four hours after attack of severe substernal pain, shows that the T wave in Lead CR_4 is plus-minus diphasic. *B* was taken May 7, 1940, eighteen hours after severe attack of substernal pain; the T wave in Lead CR_4 is still diphasic, but of decreased amplitude. *C* was taken April 29, 1941, after dietary and medical treatment, and is normal. *D*, taken Feb. 3, 1944, is normal in all four leads.

CASE 3.—*History.*—A physician, 57 years of age, had attacks of substernal, squeezing distress which occurred with or without exertion and had been present over a period of twelve years. These pains were associated with definite abdominal distress, bloating, and belching. Of late years the substernal, squeezing pain had been accompanied by an ache in both arms. Certain foods, as well as exertion, would precipitate an attack, and rest or a sedative would usually bring relief. He had had an attack of acute cholecystitis twenty-five years before, and ten years before was told that he had coronary occlusion and would not live six months. In August, 1941, while walking, he suffered his most severe attack of constricting substernal pain which did not radiate, and was associated with marked gastric distress. Standing still gave relief, but he was able to walk several blocks to his home. He perspired profusely, vomited, and required morphine; he was in a state of mild shock. He felt perfectly well the next morning, and his later recovery was rapid and uneventful.

Examination.—He was first examined in March, 1941, during an attack of substernal pain. He was pale and emotionally disturbed, the pupillary and tendon reflexes were normal, the teeth were in poor condition, the heart rate was 48, and the blood pressure was 125/80. The lungs were normal, and the heart was of normal size; its rate was slow, the sounds were good, the accentuations at the base were normal, and there were no murmurs. There was distinct tenderness in the upper right quadrant of the abdomen, but no palpable masses or viscera, and the extremities were negative. During his acute attack in August, 1941, the blood pressure was elevated to 160/74, while the pulse rate remained at 48. His leucocyte count was 14,000, with a normal differential count, and the count dropped to 7,600 within thirty-six hours. There was no rise in temperature. Several weeks after this acute attack, cholecystograms were reported as showing evidence of chronic cholecystitis.

Electrocardiogram.—His first electrocardiogram, Fig. 3, *A*, was taken May 9, 1940, and shows bradycardia and slight elevation of the R-T segment in Lead I and a normal CR_4. Fig. 3, *B*, was taken twelve hours after his severe attack of substernal pain in August, 1941, and shows slight elevation of the R-T segment in Lead I, depression of the same segment in Lead III, a plus-minus T wave in Lead I, and a minus-plus T wave in Lead III. The T wave in CR_4 shows the same plus-minus change. Fig. 3, *C*, taken three days later, on Aug. 13, 1941, shows similar, but less marked, changes in the T waves of Leads I, III, and CR_4. Fig. 3, *D*, was taken Nov. 23, 1943, and reveals normal limb leads and a normal CR_4; the amplitude of the R wave has returned to its former normal, and the T wave is upright.



A. *B.* *C.* *D.*

Fig. 3.—Diagnosis: acute cholecystitis. *A* was taken May 9, 1940, and shows bradycardia, but otherwise is normal. *B* was taken Aug. 9, 1941, twelve hours after attack of severe substernal pain; the R-T segment is elevated in Lead I and depressed in Lead III; T_1 shows plus-minus, and T_3, minus-plus inversion; in CR_4 the R-T segment is isoelectric and the T wave shows a plus-minus inversion. *C* was taken Aug. 13, 1941, and shows bradycardia and similar, but less pronounced, changes in the T waves of Leads I, III, and CR_4. *D*, taken Nov. 23, 1943, is normal; the R wave in CR_4 which was decreased in the electrocardiogram of Sept. 25, 1941, has assumed its former amplitude.

DISCUSSION

There are many conditions which temporarily alter the electrocardiogram. Recently, Scherf, et al.,[3] have discussed electrocardiographic changes which they attribute to acute hemorrhage from duodenal ulcers. However, they observed that the electrocardiographic changes were not altered by transfusions, nor did they bear any relationship to the hemoglobin content of the patients' blood.

Acute inflammatory and ulcerative conditions involving the gall bladder or duodenum cause irritation and spasticity of surrounding structures and create stimuli which act reflexly through autonomic pathways[1] to restrict or in some other manner alter the coronary blood supply, so that existing minor deficiencies in the coronary circulation become manifest. It seems probable that people with acute duodenal or gall bladder disease whose electrocardiograms show the transient changes I have described do have minor alterations in their coronary circulation; otherwise, all people with such acute conditions would show similar electrocardiographic patterns.

These cases are presented not to deny the presence of coronary artery disease, but to show that acute upper abdominal disease can prematurely reveal subclinical changes in the coronary circulation. This characteristic pattern in the electrocardiogram should not be interpreted as indicating coronary occlusion. Others have observed the relationship between the gastrointestinal tract or gall bladder and cardiac symptoms.[4-7]

In Case 3, with acute gall bladder disease, the existing changes in the coronary circulation or the reflex stimulus may have been greater or of longer duration than in the others, and, accordingly, the temporary change in the electrocardiographic pattern involved not only the chest lead, but the limb leads as well. However, if there was any disease of the coronary arteries or a diminished coronary circulation, it was still below a clinically diagnosable level, and was revealed by an upper abdominal disease crisis. The alterations in the electrocardiogram were caused by temporary myocardial ischemia and in all instances disappeared.

It is debatable whether chronic or acute gall bladder disease is harmful to the heart. I believe that these cases show that it can be an aggravating factor in heart disease. The repeated crises of the abdominal disease, with temporary embarrassment of a possibly, although slightly, altered coronary circulation, certainly influence the future welfare of that heart. These records suggest a diagnostic change in the electrocardiogram, and point out the desirability of prompt corrective measures to safeguard such patients against repeated disturbance of their coronary circulation.

CONCLUSIONS

1. Three instances of syndromes like coronary occlusion which were induced by acute upper abdominal disease are reported.

2. A constant, but not persistent, change was noted in the T waves of the electrocardiograms.

3. The relationship of upper abdominal disease and heart symptoms is discussed.

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MOMENTARY ATRIAL ELECTRICAL AXES

III. A-V Nodal Rhythm

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WE HAVE previously described the patterns obtained by graphing in three dimensions the consecutive momentary atrial electrical axes in sinus rhythm[1] and in atrial flutter, atrial fibrillation, and paroxysmal tachycardia.[2] Using the same methods we have obtained similar data from patients with A-V nodal rhythm.

Typical A-V nodal rhythm is characterized in man by the presence of negative P waves in Leads II and III of the electrocardiogram. Since the early experiments of Ganter and Zahn[3, 4] and Meek and Eyster,[5] the position of the P wave in relation to the QRS complex has been taken to indicate the position of the nodal pacemaker in the upper, middle, or lower portions of the A-V node, with atrial excitation occurring before, with, or after ventricular excitation, respectively. Scherf[6] conceived that a change in the position of the pacemaker was not essential to variation in the relation of the P wave to the QRS complex, but that delay in infranodal conduction might cause a positive P-R interval in cases in which atrial and ventricular complexes would otherwise have been superimposed. Rothberger and Scherf[7] found that the speed of retrograde conduction from the node to the atria might affect the relative position of the P and QRS complexes in experimental animals. Recently, Langendorf, Simon, and Katz[8] have cited clinical examples which suggest that the relative speeds of retrograde and antegrade conduction from a single nodal pacemaker may explain the variable positions of the atrial and ventricular complexes.

A distinct variety of nodal rhythm is that in which the P waves are upright in all leads, with a P-R interval of 0.12 second or less. This is often referred to as a "coronary" nodal rhythm, and the pacemaker is assumed to reside in those ramifications of the A-V node which adjoin the coronary sinus. The statement that at least 0.12 second is consumed in the passage of the impulse through the nodal tissue to the ventricles implies as a corollary that the pacemaker must be within the node whenever the P-R interval is equal to, or less than, that figure. Other alternative interpretations will be discussed later. This type of nodal rhythm is not uncommon clinically.

On the other hand, A-V nodal rhythm with negative P waves in Leads II and III is rare, and often transient. We have been able to study five examples of this mechanism by means of chest leads so placed that the Einthoven triangles which were formed lay in the frontal, horizontal, and sagittal planes.[1] Our earlier experience with this method led us to the conclusion that the curves and three-dimensional models constructed from such electrocardiographic data might be modified by changes in the site of the pacemaker, in the position of the heart, or by the quality of the myocardium as a conducting medium. In this paper we are concerned chiefly with the demonstration of the sequence of atrial excitation when the pacemaker of the heart is in the A-V node, as reflected in the sequence of changes of the mean atrial electrical axes.

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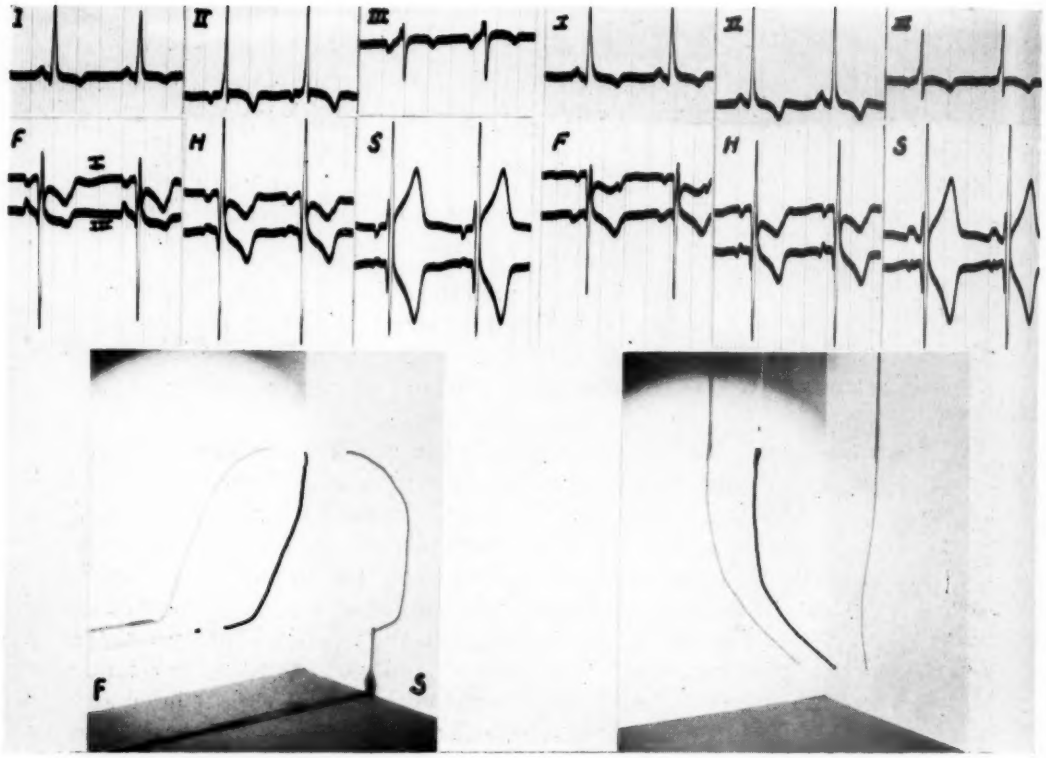

Fig. 1.—A-V nodal rhythm; sinus rhythm. In each of the figures the conventional limb leads are shown on the upper line. Below are the simultaneously recorded Leads I and III in the frontal (F), horizontal (H), and sagittal (S) planes, placed in that order from left to right. In the photograph below the electrocardiograms, the black wire represents the direction of movement of the atrial electrical axes for consecutive intervals of 0.01 second. The shadows cast by the wire reproduce the graphs obtained for the frontal and sagittal planes.

In Fig. 1, the group at the left represents the consecutive atrial axes during A-V nodal rhythm; that on the right represents sinus rhythm in the same patient.

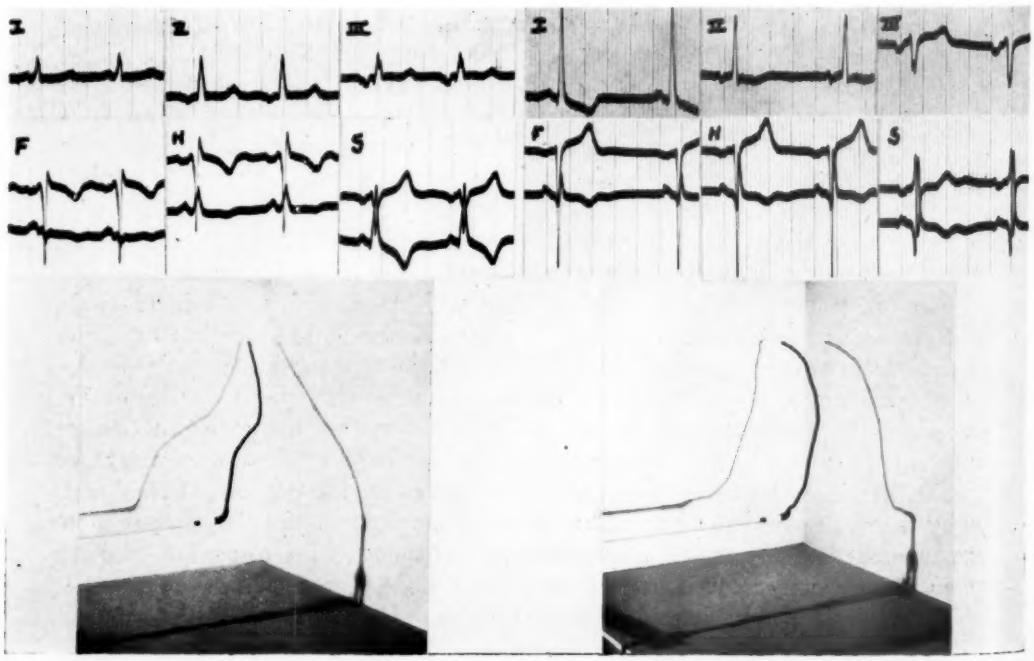

Fig. 2.—The direction of the consecutive atrial electrical axes in two additional cases of A-V nodal rhythm.

EXPERIMENTAL RESULTS

Cases in Which There Were Negative P Waves in Leads II and III.—Fig. 1 contrasts the curve of the momentary axes when the pacemaker is in the A-V node with that obtained when the impulse originates in the S-A node. In normal hearts with sinus rhythm the curves usually run smoothly down, variably forward, and to the left.[1] In this case the curve during sinus rhythm is not clearly abnormal, and, although it deviates slightly from the average in running down, slightly backwards, and to the left, this is within the normal range of variation. When the pacemaker is within the A-V node, however, the curve is strikingly changed, passing up, backwards, and to the left. Two additional instances of A-V nodal rhythm are illustrated in Fig. 2, in both of which the curves are similar to that of Fig. 1, i.e., are directed up, back, and to the left.

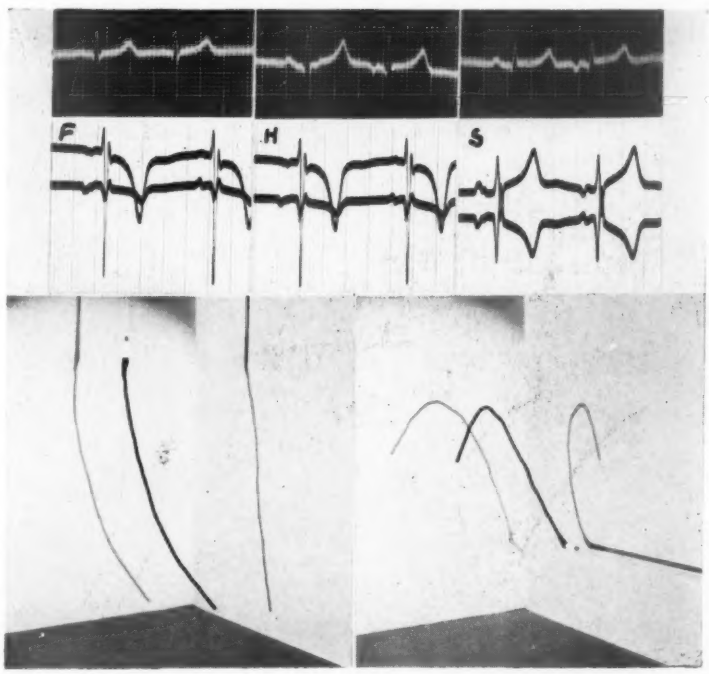

Fig. 3.—Sinus beat; atrial premature beat. Electrocardiograms and models of a sinus beat, followed by a premature beat of atrial origin.

Fig. 3 illustrates the data obtained from a patient who had premature beats which we, at first glance, thought might arise in the A-V node, inasmuch as the P waves of the premature beats were negative in Leads II and III. Analysis of the electrocardiograms obtained in the three planes, with construction of the three-dimensional model shown, indicates that the mean electrical axes pass, from moment to moment, up and to the right, and later pass down, forward, and to the right. The sinus beats gave a normal curve. This indicates to us that the premature beats probably arose in an ectopic focus located in the lower part of the left atrium. These observations also indicate that negative P waves in Leads II and III do not necessarily place the pacemaker in the A-V node. Whenever the ectopic focus is in such a position that the spread of excitation is cephalad, as in the atrial premature beat analyzed by Schellong[9] with special frontal plane leads, the projection of the mean electrical axis on Leads II and III will be such that the P waves in these leads will be negative. We would have

anticipated that the P of Lead I would have been negative in this case, but it is virtually isoelectric.

"Coronary" Nodal Rhythm.—In Fig. 4 we have shown the electrocardiograms, and models constructed from them, derived from two patients with the so-called "coronary" type of nodal rhythm. In these instances the P-R interval is 0.10 and 0.11 second, respectively. The curves in these cases differ in no way from those obtained from patients with sinus rhythm; both curves point down, forward, and to the left. This indicates that the spread of excitation over the atria is similar in "coronary" nodal rhythm to the spread in sinus rhythm, insofar as this may be deduced from the consecutive electrical axes. It also suggests that the site of the pacemaker, or rather the point at which the impulse enters the atria, is very little different in the two types of rhythm, if, indeed, there is any difference at all. The question logically arises as to whether or not this variety is genuine nodal rhythm, with the pacemaker within the A-V node. This question has been raised before, and will be elaborated upon.

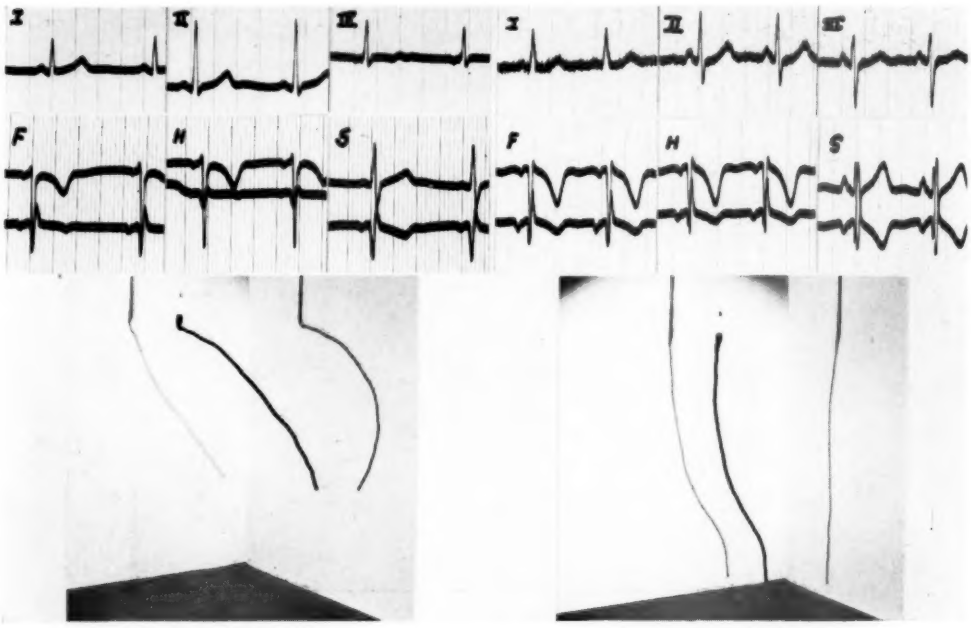

Fig. 4.—Two examples of "coronary" nodal rhythm; see text.

DISCUSSION

Atrioventricular nodal rhythm was first described by Engelmann,[10] who observed almost simultaneous atrial and ventricular contraction after exclusion of the S-A node by the first Stannius ligature; he assumed that under these circumstances the pacemaker of the heart was on the ventricular side of the A-V ring. Lohmann[11] corroborated these conclusions in the mammalian heart. He also confirmed the Stannius-Munk phenomenon—the production of nodal rhythm by needling the A-V nodal region (Brückenfäsern).

Zahn and his associates[3, 4] later attempted to localize the seat of impulse formation more exactly within the A-V nodal tissue, and showed that the atrial rate was affected by cooling the upper part of the A-V node near the coronary sinus in those cases in which atrial preceded ventricular contraction. When atrial and ventricular contractions were simultaneous, the middle portion of the node appeared to control impulse formation, and when atrial followed ventricu-

lar contraction, the pacemaker was thought to be in the ventricular portion of the node. These experiments form the basis for the concept of upper, middle, and lower nodal rhythm. In experimental nodal rhythm, Meek and Eyster[5] found initial negativity either in the region of the coronary sinus or in the ventricular portion of the A-V node, and interpreted their results as confirming those of Zahn. Neither group of workers correlated their observations with the limb-lead P-wave patterns.

Both Lewis[12] and Scherf[13] pointed out the uncertainty of localization of portions of a small, deep-seated structure such as the A-V node. Scherf[6, 13] also critically surveyed Zahn's experimental technique, and cast doubt upon the latter's concept by failing to confirm his experimental results. Scherf found that the various experimental procedures which are calculated to produce A-V nodal rhythm almost invariably produced the so-called middle variety, the type also most commonly seen in patients. For example, he found that, after resection of the S-A node in the dog more completely than had been accomplished by Zahn, the P and QRS complexes were superimposed in ten experiments, there was a short P-R interval in two, and a negative P-R, or R-P, interval in two others. Further warming of the higher portions of the A-V node failed to accelerate the rate, or to produce a positive P-R interval when superimposition or an R-P interval was present. In fact, in the two cases in which there was a short, positive P-R interval, warming of the upper portion of the A-V node caused the P wave to merge with the QRS. Scherf concluded that conduction is slower to the atrium (retrograde) than to the ventricle, thus explaining the shortening of the P-R interval. Langendorf, Simon, and Katz[8] have elaborated this concept to explain all three types of nodal rhythm as the result of variation in the relative speeds of conduction from the nodal pacemaker to the atria and ventricles. Our own[14] studies of varying rates of retrograde conduction, both spontaneous and under drug influences, would lead us to concur in the idea that variable retrograde conduction determined the position of the P wave in relation to the QRS complex. Retrograde conduction was, we found, more markedly affected by drugs than was forward conduction, although, of course, changes in the latter might readily play a role in determining the position of the P wave.

Quite recently, Scherf,[15] in pursuit of his earlier efforts to produce A-V nodal rhythm by stimulation of the coronary sinus branches of the node, reported that warming the coronary sinus on the epicardial surface produced nodal tachycardia, with negative P waves preceding the QRS in Lead II. This occurred even though the same stimulus had failed to produce negative P waves preceding the QRS, when applied to the endocardial surface. The P-R intervals were not short, but were equal to, or longer than, the P-R intervals during sinus rhythm. This is referred to as an "upper auriculoventricular rhythm (coronary sinus rhythm)," and is not comparable to the "coronary" nodal rhythm with upright P waves described below. We have pointed out above that the P waves may be negative in Leads II and III whenever the impulse spreads in a cephalad direction, e.g., the case illustrated in Fig. 3. It is to be anticipated that any impulse arising near the A-V ring would spread in this fashion. We have found that in human A-V nodal rhythm the direction of the impulse is cephalad, and also back and to the left. It remains to be proved that the impulse from the point stimulated by Scherf will spread in this fashion; we would expect it to spread forward rather than backward.

Middle nodal rhythm would not, of course, be susceptible to analysis by our method, for no P waves are visible. We have had no case with retrograde P waves available for study, but are confident from the contours of the P waves

in the limb leads that the results would not differ from those in cases in which P waves precede the QRS. We feel justified in assuming that, whether the pacemaker shifts in the A-V node, or, as seems more likely, the speed of retrograde conduction is the chief variable, the retrograde pathway is usually so situated that the impulse enters the atria at such a point that the spread of excitation, as judged by the directions of the consecutive mean electrical axes, is up, back, and to the left. The fact that variable retrograde pathways have been postulated[14, 16] does not invalidate this generalization.

The term "coronary" nodal rhythm was first employed by Edens;[17] since his studies were all on venous pulse tracings, it is doubtful whether he used it in the sense in which it is now understood, viz., upright P waves in all three limb leads, with a P-R interval of 0.12 second or less.[18] Clere and Pezzi[19] described a supraseptal rhythm, but again all of the records were mechanical. Meek and Eyster[5] found initial negativity in one of two places, usually in the ventricular portion of the A-V node or near the coronary sinus, in escaped beats during vagus stimulation in the dog, but here again there was no correlation with the form of the P waves in the limb leads.

At present the term is employed for tracings with upright P waves in all leads, but with a P-R interval of 0.12 second or less. Absence of the typical pattern of retrograde conduction, i.e., negative P waves in Leads II and III, has necessitated many hypothetical attempts at explanation. Assuming that the pacemaker in such cases actually lies in the A-V node, the upright P waves might be explained as a result of (1) intra-atrial block, producing a pathway similar to that of sinus beats; (2) a variable retrograde pathway through a ramification of the A-V node near the coronary sinus or the S-A node, and different from the one traversed by impulses giving the usual negative P waves in Leads II and III; or (3) location of the pacemaker in fibers of the A-V node near, or to the right of,[8] the coronary sinus (hence "coronary" nodal rhythm). On the other hand, if the pacemaker in these cases is supranodal, it might lie in (1) islands of S-A nodal tissue[20] or ramifications of the S-A node in the neighborhood of the coronary sinus; (2) in the tail of the S-A node, nearer the A-V node than normal; or (3) in the usual position in the S-A node, but with unusually rapid conduction (a) from the S-A to the A-V node, possibly through special functional pathways, or (b) through the A-V node.

Rothberger and Scherf[7] and Condorelli[21] found that negative P waves could be associated with sinus rhythm, and, conversely, that positive P waves might be seen in A-V nodal rhythm, facts which they explained as the result of variable intra-atrial conduction. The usual retrograde pathway from the A-V nodal pacemaker enters the atrium at a point which gives the type of curve shown in Fig. 2. We have described variation in the retrograde pathway which is sufficient to give alternation of the P waves.[14] It is conceivable that the impulse traverses those fibers which lie near the coronary sinus, and, in effect, enters the atrium in the same fashion as it would have, had the impulse actually originated in the fibers of the A-V node near, or to the right of, the coronary sinus.

Holzmann and Scherf[20] had a single animal whose S-A node had been cut away, in which they were able to produce positive P waves, just preceding the QRS complexes, by warming the mouth of the coronary sinus. This same animal later yielded negative P waves, as did their other animals. They were inclined to regard these exceptional results as being due to the presence of isolated islands of S-A nodal tissue in the vicinity of the mouth of the coronary sinus.

Our data, as depicted in Fig. 4, indicate that the spread of excitation over the atria in "coronary" nodal rhythm is indistinguishable from that in normal sinus rhythm. We infer from this that the impulse enters the atria in approximately the same place in both conditions. The normal, smooth contours of the curves fail to provide any evidence for the presence of a conduction defect with intra-atrial block, and indicate that such a disturbance of conduction is not the cause of the upright P waves. Nor do they support the view favored by Langendorf, et al.,[8] that upright P waves with short P-R intervals arise from proximal fibers of the A-V node, lying to the right of the coronary sinus. We are accustomed to thinking of the upper fibers of the A-V node as being closely related functionally to the S-A node, with the pacemaker moving to the former when the latter is depressed. Although experimental proof of such a concept is far from convincing, of more importance to us at the moment is the fact that anatomically these two areas are well removed from each other. We would anticipate that impulses arising from the neighborhood of the coronary sinus would spread quite differently from those springing from the S-A node, and would yield entirely different patterns when the consecutive atrial electrical axes were graphed. Of course, experimental evidence would be necessary to prove the truth of this conjecture, but it receives some support from Scherf's recent paper.[15]

Lewis felt that the excitation wave spread concentrically from the S-A node throughout the atrial muscle, stimulating the A-V node in passage. There is some evidence, however, of specialized functional pathways within the atrial musculature. Meek and Eyster, Rothberger and Scherf, and Condorelli found evidence of a special connection between the two nodes; these pathways were not demonstrable anatomically, but were considered to be functional pathways. These claims might give substance to the possibility that shortening of the P-R interval below 0.12 second in sinus rhythm might be due to acceleration of conduction along such a pathway. Consideration of the fact[12] that only about one-third or one-fourth of the P-R interval is required for excitation of all the atrial muscle, and that presumably much less than this is occupied in passage of the impulse to the A-V node makes it seem unlikely that any appreciable shortening of the P-R interval could be due to acceleration of intra-atrial conduction.

It is well established that the major delay in atrioventricular conduction occurs in the A-V nodal tissue.[12] The length of time usually required for passage of the A-V junction is probably more than one-half of the P-R interval; more rapid conduction at this point could well decrease the P-R interval to below 0.12 second. These A-V junctional tissues are known to be most susceptible to humoral and nervous influences which affect conduction.

It is not warranted to place a lower limit of 0.12 second on the normal P-R interval, as has been done by many authors, including Scherf and Schönbrunner.[22] Recent studies have shown that among large groups of apparently normal persons the A-V conduction times follow a fairly symmetrical distribution curve. Stewart and Manning[23] have reported an analysis of the electrocardiograms of five hundred Air Corps personnel. They found that the mean P-R interval in Lead II was 0.16 ± 0.001 second; the limits of twice the standard deviation on each side of the mean were from 0.11 to 0.21 second, and, of three times the standard deviation, 0.09 to 0.24 second. Graybiel, et al.,[24] in a similar study of one thousand healthy aviators, found a mean P-R interval in Lead II of 0.154 second; this excluded two examples of short P-R interval with prolonged

QRS complexes. The latter authors accept such P-R intervals as indicating unusually rapid conduction from atria to ventricles, with less than the usual delay in the A-V junctional tissues.

It may be of interest, in passing, that the consecutive electrical axis pattern of the P wave in the short P-R, long QRS syndrome is of the usual S-A nodal type in the single case we have analyzed. Pezzi[25] considered this type of curve as an example of a supraseptal rhythm.

We believe that the evidence cited proves that the so-called "coronary" type of nodal rhythm is not a variety of A-V nodal rhythm, but is, in fact, simply normal sinus rhythm with a short P-R interval, which, in accordance with the laws of distribution, occurs relatively uncommonly.

SUMMARY

Using a method of analysis of the P wave, recorded in three planes of the chest as previously described, we have studied the curves of the consecutive momentary atrial axes in A-V nodal rhythm. In three dimensions, the curves pass up, back, and to the left.

The curves obtained in so-called "coronary" nodal rhythm resemble those of ordinary sinus rhythm, passing down, variably forward, and to the left. The available evidence is surveyed, and it is concluded that this latter type of nodal rhythm is actually merely an example of sinus rhythm with relatively rapid conduction of the impulse through the A-V junctional tissues.

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Clinical Reports

ORCHITIS AND HYDROCELE AFTER CARDIAC INFARCTION

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THE following case seems worth reporting because no similar observation has been reported.

CASE REPORT

The patient was a white man, 64 years of age. There was no previous history of illness and no history of venereal disease. In August, 1941, when the patient came under my observation, he showed definite signs leading to a diagnosis of coronary sclerosis. At that time the pulse rate was 72, and the blood pressure, 135/85; there were single ventricular ectopic beats; the electrocardiogram showed a flat T_2 and a slurred QRS complex in Leads I, II, and III. One evening in September, 1943, as he was walking on the street, he suddenly felt a severe pain in the chest, became nauseated, and began to perspire excessively. When I saw him, a half hour later, he was pale, his skin was cool but wet with perspiration, and he complained that the pain was very severe. His pulse rate was 104, and his blood pressure, 160/90. An electrocardiogram was taken immediately, and was repeated daily for the next three days. The changes in the electrocardiogram were most definite between thirty-nine and sixty hours after the attack. The S-T segment was depressed in Lead I and in the left chest lead (CR_6) and elevated in Lead III. At that time, T was inverted in Leads II, III, and the right and left chest leads (CR_2, CR_6, and CR_8). The following morning (eleven hours after the attack), his temperature was 99° F., and the next morning, 100.4°; but, from the day after that, it remained normal (less than 99°). The sedimentation rate on the day after the attack was 18 mm. in two hours, and the leucocyte count before breakfast was 13,200 (83 per cent polymorphonuclears, 11 per cent lymphocytes, and 6 per cent monocytes). The blood pressure was 110/70, and remained at this level two days; on the third day it had risen to 120/75, and a week later was 130/80, at which level it was maintained. Whereas before the attack the pulse rate was always about 70, after the attack it rose to about 100 and remained at that level during the following ten days. Single ectopic beats (nodal type) and salvos of them were present on the second day, but after that and until the present writing no more have been found.

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The patient's recovery was excellent, and he had been feeling fine, when, suddenly, on the sixteenth day after the attack described, he felt uncomfortable and complained of pain in the lower part of the abdomen. The following night he was unable to sleep, felt very restless, and complained of severe pains in the abdomen and testicles. When I saw him the next morning, the left testicle, previously normal in size, had swollen to the size of a large orange; it was very sensitive and painful, and the scrotal skin appeared tense and red. The temperature was normal (98°), and the abdomen somewhat tender, with no rigidity of the abdominal walls. That evening the temperature was 98.6°; no higher temperature was found in the following days. The pulse rate, which had ranged between 76 and 80 in the previous days, had risen to 96; the blood pressure was 135/80. There was no swelling of the parotid gland, nor was there any history of exposure, in the weeks previous, to the mumps. A modified suspensory was applied and cool compresses recommended. The following day the pulse rate was 90, and the day after that, 84. In the course of a week the pain gradually was relieved and the size of the testicle reduced, but the hydrocele remained quite obvious and identifiable as a light-translucent swelling of the left testicle alone. During the next three weeks the testicle shrank to about half the size it had displayed on the occasion when it had swelled and caused so much pain; nevertheless, it remained definitely and abnormally enlarged as compared with the normal one. In the meantime, the heart condition had improved so well that, after the sixth week, the patient was able to stay out of bed and later felt sufficiently comfortable to return to his normal occupation as a research worker.

The most satisfactory explanation for this series of events seems to be as follows. A small mural thrombus due to coronary occlusion gave rise to an embolism which produced the symptoms described. As is well known, emboli in other parts of the body are not rare occurrences after cardiac infarction.

SUMMARY

This case is unique in that, on the sixteenth day after indubitable cardiac infarction, orchitis and hydrocele developed in conjunction with intense abdominal pain. The explanation offered for this picture is embolism due to mural thrombi caused by cardiac infarction.

SILICOSIS OF THE PERICARDIUM

Case Report

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RECENTLY we[1] completed a study of sixty-four cases of silicosis and silicotuberculosis. In a few of these, silicotic foci were found in the spleen and liver, apparently as a result of hematogenous dissemination of siliceous particles. However, in the majority, the silicotic foci were limited to the lungs and draining lymph nodes, and in no case was there evidence of lymphatic dissemination to any other organ of the body. Since the completion of this study,

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we have observed three additional cases of silicosis and silicotuberculosis. In one of these, silicotic foci were found in the visceral pericardium and were apparently the etiological factor in the production of a noninfectious adhesive pericarditis. Since there was no evidence of silicosis in the myocardium, the lymph channels were probably the routes for the dissemination of the dust. In addition to the rarity of silicosis of the pericardium, this case illustrated the communication between pleural and pericardial lymphatic vessels.

CASE REPORT

History.—The patient, F. F., was a 51-year-old white man, a Spaniard by birth and a stonecutter by trade. He had noticed frequent "colds" and increasing dyspnea since 1936 and, in March, 1941, "streaked" blood for the first time. His local doctor diagnosed silicotuberculosis and instituted pneumothorax on the left side. He stopped work, remained at home, and was treated by the reinstitution of pneumothorax irregularly until November, 1942. At this time he had a large hemoptysis and was hospitalized; he was finally admitted to Sea View Hospital on Jan. 8, 1943. Since March, 1941, he had lost 22 pounds in weight and had experienced progressively increasing dyspnea. His past medical and family history were irrelevant.

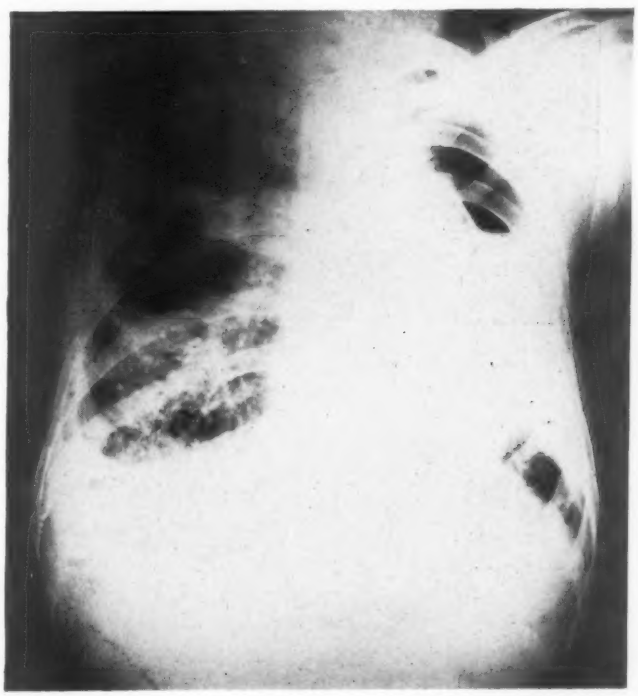

Fig. 1.—Roentgenogram made July 9, 1943. Encapsulated hydropneumothorax on the left. Marked retraction of the heart and mediastinum to the left. Spread to the right radiating from the hilum.

Physical Examination.—The patient was a well-developed, poorly nourished adult who appeared chronically ill. He was markedly dyspneic, but not cyanotic. There was moderate clubbing of the fingers. Other abnormalities were limited to the chest. There were signs of hydropneumothorax on the left side, with râles and bronchial breathing over the left upper lobe. The right lung was normal. The heart was normal in size, the rate was 90 per minute, and the rhythm was normal. There was a soft systolic murmur at the apex, transmitted to the axilla.

The urine had a specific gravity of 1.010 and was normal except for occasional leucocytes. The blood Wassermann reaction was negative. The erythrocyte count was 4,100,000, the hemoglobin, 78 per cent, and the leucocyte count, 8,500, of which 68 per cent were polymorphonuclear leûcocytes, 3 per cent nonsegmented polymorphonuclear leucocytes, 17 per cent lymphocytes, 8 per cent monocytes, 1 per cent eosinophiles, and 1 per cent baso-

philes. The sedimentation rate was 74 mm. in forty-five minutes. The sputum contained tubercle bacilli, Gaffky VII. The blood glucose and nonprotein nitrogen levels were normal.

A roentgenogram of the chest (Fig. 1) revealed almost complete collapse of the left lung, with encapsulated fluid at the level of the eighth rib posteriorly. In the right lung there was a diffuse, nodular type of infiltration throughout, more extensive in the upper and middle portions.

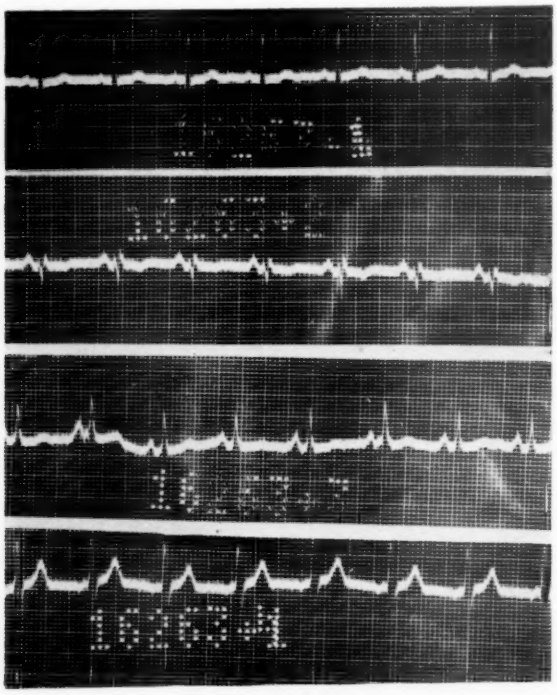

Fig. 2.—Electrocardiogram in July, 1943. Slurring of QRS complex and inversion of T wave in Lead II, with essentially normal tracings in other leads, indicative of cardiac rotation rather than myocardial damage.

Fig. 3.—Coronal section of the lungs. Silicotic foci throughout, many with secondary caseation. Compressed, interlocking excavation in left upper lobe. Almost entire left lung fibrotic and contracted. Left empyema space, with dense pleuropericardial adhesions.

Course.—Because of the dyspnea and the ineffectiveness of the pneumothorax, the latter was discontinued. Six weeks after admission, generalized petechiae of the lower extremities appeared. The platelet count at this time was 289,720, and the blood picture was essentially the same as on admission. The liver and spleen were not felt, and the petechiae disappeared spontaneously after about four weeks. The electrocardiogram at this time showed inversion of the T wave and slurring of the QRS complex in Lead II. Since there was retraction of the heart into the left side of the chest, with probable rotation, this could not be interpreted as evidence of myocardial damage (Fig. 2).

In spite of aspiration of fluid from the left pleural sac, the patient became increasingly dyspneic. In April, 1943, the temperature rose to 101° to 102° F., and there was evidence of extensive bronchogenic spread to the right lung. On Sept. 7, 1943, he spat up two ounces of blood, and died Oct. 12, 1943, of progressive pulmonary insufficiency. Terminally there were marked dyspnea and cyanosis, but no edema. The abdomen was soft, but diffusely tender. No solid organs were palpable.

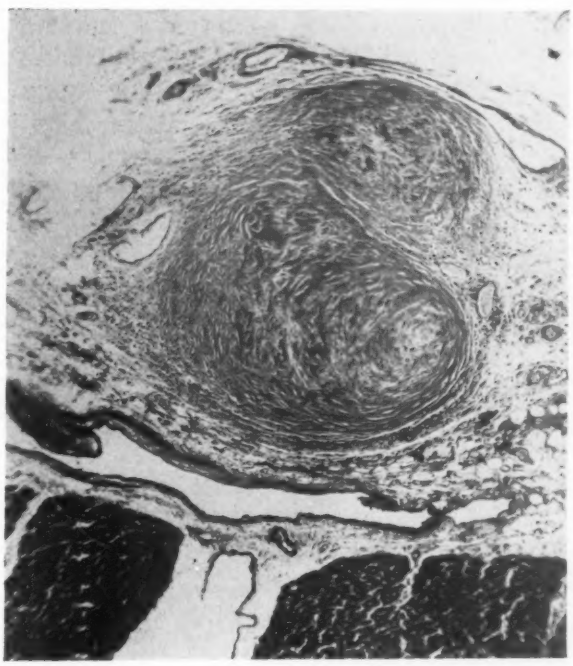

Fig. 4.—Photomicrograph of left ventricle. Silicotic focus in the pericardium adjacent to a large blood vessel at the site of dense adhesive pericarditis. No foci in the myocardium.

Autopsy.—The lungs weighed 3,510 grams. The small, residual left pleural space was filled with 300 c.c. of yellowish-green fluid containing large amounts of fibrin. The pleural space was obliterated over most of the left lung, and the visceral and parietal pleurae were markedly thickened. The pleura over the right lung was also thickened, although to a less extent, and the pleural space was completely obliterated. Section of the left lung showed that it was almost completely occupied by conglomerate silicotic foci (Fig. 3). In the left upper lobe there was a large, elliptical, tuberculous excavation measuring 7.5 cm. in its largest, apicobasal direction. The right lung was studded with silicotic foci measuring from 3 to 10 mm. in diameter. A tuberculous cavity, 1 cm. in diameter, was present in the upper lobe. The tracheobronchial and peribronchial lymph nodes were from 1 to 3 cm. in diameter and were almost completely occupied by silicotic foci.

The heart, without the pericardium, weighed 360 grams. The pericardial cavity was completely obliterated by thin, fibrous adhesions, except over the atria and a portion of the left ventricle posteriorly, where the adhesions were thick, firm, and impossible to separate except by sharp dissection. The parietal pericardium was adherent almost completely to the left parietal pleura posteriorly. A patent foramen ovale admitted the tip of a probe. The right ventricular wall measured 8 mm. in thickness, and the left, 11 millimeters. There was moderate atheromatosis of the coronary arteries and aorta. There was no evidence of infarction, but microscopic examination of the left ventricle in the region of the

firm, fibrous adhesions revealed silicotic foci within the visceral pericardium (Fig. 4). There were no cellular or other abnormalities suggestive of an infectious process in the pericardium. There were no silicotic foci in the myocardium.

Other lesions included miliary tubercles of the spleen and kidney and tuberculous ulcerations of the ileum and larynx. The liver weighed 1,640 grams, and the spleen, 375 grams. The peripancreatic lymph nodes contained silicotic foci similar to, but less extensive than, those of the tracheobronchial nodes.

COMMENT

In their extensive studies of pneumoconiosis, Gardner,[2] Cummins,[3] and others have repeatedly emphasized the importance of blockage of the lymphatic channels by dust thrombi and the resulting fibrosis. Since, however, this blockage probably occurs chiefly in the lymphatic vessels of the tracheobronchial nodes, there remains a possible exit for silica particles in the peripheral (pleural) lymphatic vessels. Although retrograde lymph flow from the tracheobronchial nodes along the afferent channels from the pericardium is possible, the early obstruction within the nodes makes this unlikely. Since the lymphatic vessels from the peripheral portions of the lungs, which are affected by silicosis last, drain towards the pleura and not the hilum, they may remain patent long after the deep lymphatic vessels have been blocked.

These superficial lymphatic vessels, like those of the deep channels of the lung, the heart, and the pericardium, ultimately reach the mediastinum. However, when the pleura and pericardium are adherent there is probably free communication between the lymphatic vessels of the two. This was true in this case; the adhesions were present over a wide area posteriorly. Obviously, the more extensive the adhesions between the pleura and pericardium, the greater will be the lymph exchange. How extensively the adhesions develop depends chiefly upon the pulmonary lesions. In this case there was almost complete destruction of intrapulmonary elastic fibers by a combination of silicotic and tuberculous fibrosis. Because of its loss of resiliency, the lung occupied a much smaller space than previously, and the mediastinal structures were retracted into the left side of the chest, giving the pericardium greater opportunity to adhere to the pleura.

Neither the retraction nor the pleuropericardial adhesions are uncommon in tuberculosis, particularly with left-sided involvement. In uncomplicated silicosis and in silicotuberculosis, however, since the lungs are usually voluminous, marked retraction is unusual. The encapsulated pneumothorax in this case was large enough to augment the intrapulmonary tendency of the lung to retract, but not great enough to prevent the heart's being withdrawn into the left hemithorax.

Why the silicosis of the pericardium should lead to adhesive pericarditis is difficult to understand. The firmest attachments were at the site of the densest pleuropericardial adhesions, at which point the pleura and both the visceral and parietal pericardium were as one. Probably both the physical and irritative characteristics of the siliceous particles were responsible for the development of these adhesions.

Except for the abnormal electrocardiogram, there was no subjective or objective evidence of cardiac disease. It is likely, however, that, had the patient survived, the pericardial silicosis would have progressed, as silicosis progresses in the lungs and lymph nodes, and cardiac embarrassment might have developed.

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CONGENITAL TRICUSPID INSUFFICIENCY

Report of a Case

Viola G. Brekke, M.D.*
Detroit, Mich.

CONGENITAL tricuspid insufficiency is a rare cardiac anomaly. In an analysis of one thousand cases of congenital cardiac disease, Abbott[1] listed five cases of congenital tricuspid insufficiency in which this defect was classified as the primary lesion. She described two anatomic types of this lesion: (1) incomplete differentiation of the cusps, and (2) the Ebstein type in which the undifferentiated tricuspid segments are represented by a membranous diaphragm displaced downward toward the apex of the right ventricle. The latter type, first described by Ebstein in 1866, is a well-defined lesion. Sixteen cases belonging to this group are recorded in the literature. These cases present various degrees of differentiation of the tricuspid segments, but common to all of them is the abnormal position of the malformed segments. The segments are not located around the right atrioventricular orifice, but are displaced downward toward the apex of the right ventricle, so that a portion of the right ventricle is drawn into the right auricle, and both chambers are dilated. In all but two cases, this anomaly was associated with patency of the foramen ovale.

A case of congenital tricuspid insufficiency of the Ebstein type is reported.

REPORT OF CASE

The patient, a white, 8-month-old, female infant, was well until a few days before admission to the hospital. At that time she developed an infection of the upper respiratory tract and became dyspneic and cyanotic. The mother stated that prior to this illness the patient had become cyanotic only during crying spells.

On admission the temperature was 97° F., the pulse rate, 160, and the respirations, 78. Examination of the chest revealed no abnormality of the lungs. There was marked enlargement of the heart. No definite murmurs were heard. The cardiac rhythm was regular.

Roentgenologic studies of the chest revealed marked enlargement of the cardiac silhouette involving both ventricles, but particularly the right. The lungs were normal, and there was no evidence of obstruction of the trachea or narrowing of the bronchi. The hemoglobin was 78 per cent; the erythrocyte count was 4,100,000 per c.mm.; and the leucocyte count was 12,200 per c.mm., with 41 per cent neutrophiles.

The patient remained cyanotic after admission to the hospital, and became increasingly dyspneic. She was given oxygen continuously, and died three days after admission.

Post-mortem examination revealed a well-nourished, 8-month-old, white female infant showing cyanotic discoloration of the face, neck, and extremities, but no external malformations.

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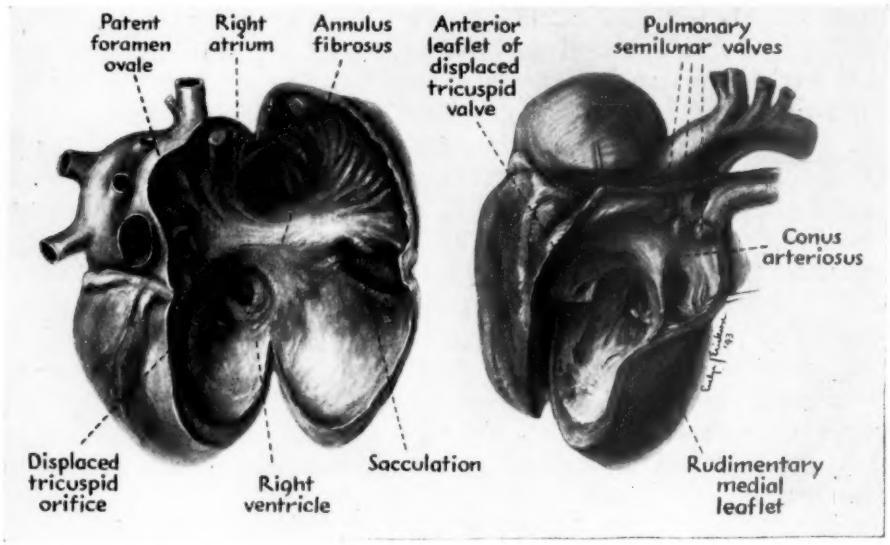
There was no fluid in the pleural cavities. Each lung weighed 50 grams. Crepitation was diminished in the lower lobes. A moderate amount of blood exuded from the cut surface.

The thymus was normal in size and appearance.

The pericardial sac was normal in appearance, and contained no excess fluid.

The heart, which weighed 53 grams and measured 5.5 cm. in its greatest transverse diameter, showed marked enlargement of the right auricle and right ventricle and a rounding of the apex. The interventricular and atrioventricular sulci were distinct. Opening the heart revealed patency of the foramen ovale; it measured 1.2 cm. in its greatest diameter. The right auricle was hypertrophied and its wall well trabeculated. The right atrioventricular orifice, 7 cm. in circumference, showed no tricuspid leaflets around its margin. A fibrous ridge extended along the posterior septal margin of this orifice and became continuous with the base of a membranous leaflet which was deflected medially and attached to the anterior wall of the conus arteriosus. The free border of this membrane formed the lateral margin of an orifice leading into the conus arteriosus. This membranous structure, which represented the anterior leaflet of the malformed and displaced tricuspid valve, divided the right ventricle into two portions. The larger portion was thrown into the cavity of the right auricle, and the remaining portion formed a smaller chamber which



A. *B.*

Fig. 1.—*A*, Drawing of the right atrium and ventricle, which have been opened to show the absence of tricuspid segments around the atrioventricular margin. Note the abnormal position of the tricuspid orifice produced by the malformed segments. *B*, Drawing of the right ventricle, which has been opened through the displaced tricuspid orifice to show the malformed segments and the separation of the right ventricle into two chambers.

included the conus arteriosus. The orifice leading into the second chamber was bounded laterally by the membranous leaflet, and medially by a fibrous ridge which extended along the interventricular septum to the anterior wall of the conus arteriosus. Below the fibrous ridge on the septum was a small pocketlike mass of endocardial tissue which represented the rudimentary septal leaflet of the tricuspid valve. The posterior leaflet was entirely unformed. There were no defects in the interventricular septum. The pulmonary orifice measured 8 mm. in circumference, and its cusps were normal. There was a saccular outpouching of the posterior lateral wall of the right ventricle, which in this area was very thin. The posterior portion of the interventricular septum was well trabeculated, but the remainder of the right ventricle had a smooth, dull lining. Examination of the left ventricle showed that the mitral leaflets, chordae tendineae, and papillary muscles were normal in appearance. The aorta and great vessels showed no abnormalities. The ductus arteriosus was closed and persisted as a thin fibrous cord.

The peritoneal cavity contained no free fluid. The liver weighed 25 grams, and a large amount of blood escaped from the cut surface. The other organs showed no gross abnormalities.

COMMENT

In this case, as in similar cases which have been reported, the anomaly involved only the right atrioventricular valve. Similar cases have been reported by Ebstein,[2] MacCallum,[3] Heigel,[4] Marxsen, Geipel, Schonenberger, Malan, Morison,[5] Abbott,[6] and Arnstein.[7] These cases present various degrees of differentiation of the tricuspid segments, but the feature common to all of them is the abnormal position of the malformed segments which results in a herniation of the larger portion of the right ventricle into the cavity of the right auricle. As stated by Heigel[4] and Arnstein,[7] the similarity among the cases rests in the following facts: that the medial leaflet is incompletely formed and in most instances is represented by a rudimentary tag; that the anterior leaflet is the largest, is abnormal in shape, and in some instances is represented by a fenestrated membrane; and that the posterior leaflet is most affected in the anomaly, and, if formed at all, is rudimentary. Heigel states that these changes must be due to malformation, because an inflammatory process, even fetal, could not produce this type of anomaly so uniformly.

In the case presented, the pseudovalvular orifice below the conus arteriosus had no valvular function, so that, anatomically and functionally, this represents a true tricuspid insufficiency.

SUMMARY

An unusual cardiac anomaly, presenting defective and displaced tricuspid valvular segments and a large, patent foramen ovale, is reported. This belongs to the type of congenital tricuspid insufficiency designated as Ebstein's disease.

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2. Ebstein, W.: Ueber einen seltenen Fall von Insufficienz der Valvula tricuspidalis, bedingt durch eine angeborene hochgradige Missbildung derselben, Arch. f. Anat. u. Physiol. vol. 238, 1866.
3. MacCallum, W. G.: Congenital Malformations of the Heart as Illustrated by the specimens in the Pathological Museum of the Johns Hopkins Hospital, Bull. Johns Hopkins Hosp. **11**: 69, 1900.
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5. Morison, A. B.: Malformed Heart With Redundant and Displaced Tricuspid Segments and Abnormal Attenuation of the Right Ventricular Wall, J. Anat. **57**: 262, 1922-1923.
6. Abbott, M. E.: Blumer's Bedside Diagnosis, Philadelphia, 1928, W. B. Saunders Co., vol. 2, p. 482.
7. Arnstein, A.: Eine seltene Missbildung der Trikuspidalklappe, Virchows Arch. f. path. Anat. **266**: 247, 1927.

Abstracts and Reviews

Selected Abstracts

Gross, D.: Psychophysiologic Studies of the Cardiac Patient. Rev. méd. de Chile **68:** 258, 1944.

An attempt is made to evaluate the influence that circulation has on the brain observing the changes in psychic functions when the circulation is impaired. For this purpose the author studies the circulation time and the results of different psychic tests in patients with congestive failure and after improvement. The circulation time from arm to tongue was measured with calcium bromide. Psychic tests measured concentration, association, attention, optic orientation, and resistance to, and individual rhythm of, mental work.

This study shows that there is no exact proportion between the speed of circulation and the speed of mental functions. However, congestive failure causes a marked decrease of all mental functions, so that values of patients normally quick become similar to those of people normally slow.

A quotient between circulation time and either association time or Schulte's test is described. It gives a kind of mathematical evaluation of the single patient independent of transitory changes due to heart failure.

A. LUISADA.

Fox, T. T.: Aberrant Atrio-Ventricular Conduction in a Case Showing a Short P-R Interval and an Abnormal But Not Prolonged QRS Complex. Am. J. M. Sc. **209:** 199, 1945.

A case is presented with a short P-R interval and an abnormal but not prolonged QRS complex. Prolongation of the QRS complex was achieved through the influence of cholinergic drugs. In this manner the syndrome of short P-R interval and prolonged QRS complex was reproduced. It would therefore appear that the width of the QRS complex in this syndrome is merely an expression of the quantity of "vagus substance" available, and that the actual criteria of the Wolff-Parkinson-White syndrome are: a short P-R interval and an abnormal but not necessarily prolonged QRS complex.

In view of this, and of the available histologic evidence of the existence of an aberrant A-V conduction pathway, it is suggested that the syndrome be known as the "aberrant atrio-ventricular conduction."

AUTHOR.

Cossio, P., Vedoya, R., and Berconsky, I.: Modifications of the Electrocardiogram After an Attack of Paroxysmal Tachycardia. Rev. argent. de cardiol. **11:** 164, 1944.

The electrocardiographic alterations which appear after an attack of paroxysmal tachycardia and which constitute an electrocardiographic syndrome were studied in two personal observations and twenty similar cases found in the literature.

This posttachycardiac syndrome is characterized by negative displacement of the S-T segment, inversion and widening of the T wave, and lengthening of the Q-T interval. It appears especially after attacks of ventricular paroxysmal tachycardia (sixteen cases). A relation was found between the situation of the automatic focus which originates the ventricular tachycardia and the lead automatic focus which originates the ventricular tachycardia and the lead (I or III) in which the electrocardiographic changes appear.

A functional alteration of the automatic ventricular focus, persisting after the attack is over, may be the cause of the posttachycardiac syndrome.

AUTHORS.

Battro, A., Aguirre, R. C., and Mendy, J. C.: Electrocardiographic Studies in Heine-Medin's Disease (Poliomyelitis). Rev. argent. de cardiol. **11**: 185, 1944.

Of thirty-eight cases of poliomyelitis observed during the acute stage, four showed electrocardiographic alterations which appear to be the expression of cardiac damage. The clinical examination did not reveal any abnormality apart from a moderate tachycardia. The facts: (1) that these electrocardiographic alterations disappeared in the course of the illness and (2) that none of the eighteen chronic cases showed electrocardiographic alterations indicate that the cardiac complication was, in these cases, of a transient nature and related to the acute period of poliomyelitis.

AUTHORS.

Manning, G. W., and Stewart, C. B.: Alteration From Normal to Abnormal P-R Interval With Change in Posture. Canad. M. A. J. **51**: 546, 1944.

In three of the cases which were observed among aircrew trainees the P-R interval was reduced from 0.28, 0.24, and 0.24 seconds, respectively, to 0.20 seconds on changing from the recumbent to the sitting position. These changes occurred without any significant alteration in heart rate. In the fourth case the P-R interval was 0.40 seconds taken in the recumbent position and 0.20 seconds taken in the sitting position with no change in heart rate. Four years later there was no significant change. The P-R interval could be reduced to normal by excessive exercise in the recumbent position or by assuming the upright position.

MCCULLOCH.

Shapiro, M. J.: The Preoperative Diagnosis of Patent Ductus Arteriosus. J. A. M. A. **126**: 934, 1944.

The diagnosis of patent ductus arteriosus can be made without error. Patients should not be referred for surgical treatment unless they show the characteristic machinery murmur. The only exception to the rule is the occasional patient with a large patent ductus who may exhibit no murmurs. Patients with cyanosis and clubbing of the fingers do not have uncomplicated patent ductus. They cannot be treated surgically. Pronounced electrocardiographic changes are not part of the picture of simple patent ductus arteriosus.

AUTHOR.

Coulter, W. W., and Marcuse, P.: Acute Isolated Myocarditis. Am. J. Clin. Path. **14**: 399, 1944.

A case is reported in which a nonspecific type of myocarditis and less marked nonspecific changes in the lungs and liver were the pathologic findings. The lesions in the heart muscles were severe enough to account for the patient's sudden death after a short illness with vague symptoms.

AUTHORS.

Dawson, M. H., and Hunter, T. H.: The Treatment of Subacute Bacterial Endocarditis With Penicillin. J. A. M. A. **127**: 129, 1945.

Twenty patients with subacute bacterial endocarditis were treated with penicillin. A preliminary group of five patients was treated in 1942 and 1943, and a group of fifteen was treated in 1944. The infecting organism was a streptococcus in all instances. Heparin was employed as an adjuvant to penicillin in the treatment of the majority. While it is recognized that a long follow-up will be necessary before the ultimate outcome is established, therapy was apparently successful in fifteen of the twenty patients. All fifteen patients are now clinically and bacteriologically free from infection. In two of the remaining five patients the infection was controlled as long as penicillin was administered, but a relapse occurred when therapy was discontinued. These two patients are still in excellent general health, and it is hoped that it will yet be possible to arrange for a therapeutic regimen which will produce a satisfactory outcome. The remaining three patients succumbed. In each instance death was apparently due to a cerebral embolus. In two of the fatal cases the infection was still present at the time of death, and in

the third the situation was in doubt. Further experience is necessary before an opinion can be expressed regarding the value of heparin as an adjuvant to penicillin in the treatment of this disease.

AUTHORS.

Tinsley, C. M.: Pneumococcic Endocarditis. Arch. Int. Med. **75**: 82, 1945.

Pneumococcic endocarditis occurs in about 3 to 3.5 per cent of all pneumococcic infections and is probably responsible for about 5 to 10 per cent of deaths due to pneumococcic infections. The aortic and mitral valves are infected in 36 and 33 per cent of the cases, respectively. In only approximately 11 per cent of the cases are the valves of the right side of the heart solely involved. Antecedent valvular damage is present in a minority of the instances but is present often enough—perhaps in one-third of the cases—that it may well contribute to the development of this disease. Purpura, splenomegaly, and infarction of organs by emboli are less common than in subacute bacterial endocarditis. The ulcerative infectious process often produces fenestration of a valve cusp, with subsequent appearance of the murmur of aortic insufficiency. A thorough search for this murmur should be made in every case of pneumococcic infection which does not give evidence of rapid and complete recovery. Pneumococcemia is almost invariably present, and repeatedly positive blood cultures are presumptive evidence of the existence of this disease. The disease is usually rapidly fatal and may terminate in acute purulent meningitis. Treatment has so far been highly unsatisfactory.

AUTHOR.

Guy, P. F.: Rheumatic Fever of Childhood. Northwest Med. **43**: 166, 1944.

Problems encountered in the diagnosis of 178 cases of rheumatic fever admitted to the Children's Orthopedic Hospital of Seattle are itemized. The five manifestations of rheumatic fever are discussed and the abstract of a case history including all five is given. The onset of rheumatic fever and the frequency of a preceding episode in the 178 cases is analyzed and reference is made to the part played by the *Streptococcus hemolyticus*. The value of continuous institutional care during the toxic period is discussed. Tonsillectomy in rheumatic fever patients, the age of onset, and other observations are analyzed.

AUTHOR.

Fashena, Gladys J.: The Incidence of Rheumatic Fever in Texas With Particular Reference to the Dallas Area. Texas State J. Med. **39**: 474, 1944.

The morbidity and mortality statistics quoted from the Children's Medical Center must be interpreted with caution since there are a number of factors which serve to weight the data. The fact that a children's cardiac clinic is in operation at the center serves to attract cardiac referrals from out of town as well as from other hospitals in the city. The mortality statistics are weighted by the fact that the hospital admits no contagious diseases and relatively little traumatic or brain surgery. Nevertheless, taking all factors into consideration, we feel that certain inferences can be drawn from the material presented here.

The official mortality statistics appear to show that the 1941 death rate from rheumatic fever in Texas in the school-age period is not strikingly less than in the so-called "rheumatic fever states." The hospital data indicate that rheumatic fever can scarcely be termed a rare disease in the Dallas area. It is believed that the disease, although probably somewhat less frequent than in the northern United States, constitutes a larger cause of morbidity and mortality in the Dallas area and probably in Texas as a whole than is generally appreciated.

AUTHOR.

Bruetsch, W. L.: Late Cerebral Sequelae of Rheumatic Fever. Arch. Int. Med. **73**: 472, 1944.

A late sequel of rheumatic fever is obliterating endarteritis, which usually develops while the patient is otherwise in good health. If the vascular process involves the small meningeal and cortical vessels, gross and microscopic infarctions in the gray matter of the brain will result, producing a variety of mental symptoms.

This type of cerebral involvement has been termed "rheumatic brain disease." It represents a chronic infectious process in the same sense as rheumatic heart disease.

Although widespread and clinically manifest obliterating arteritis seems to occur in only a small number of patients with rheumatic heart disease, the possibility of the development of rheumatic endarteritis in such a person appears to be ever present.

Rheumatic fever in the form of this late cerebral sequel has been found to be an important factor in the causation of mental illness. The fact that rheumatic heart disease is several times more frequent among mentally ill patients than in persons of the general population emphasizes this contention.

Other late cerebral sequelae of rheumatic fever are rheumatic encephalitis and cerebral embolism, the latter occurring most often during auricular fibrillation in patients with mitral stenosis.

AUTHOR.

Webb, A. C.: Periarteritis Nodosa in Pregnancy. Arch. Path. **38**: 329, 1944.

Periarteritis nodosa was observed in a parturient woman whose death most probably can be ascribed to severe toxemia and puerperal sepsis. The role played by the lesions of periarteritis nodosa in relation to the death of the patient cannot be evaluated.

AUTHOR.

Smirk, F. H.: Casual and Basal Blood Pressures; IV. Their Relationship to the Supplemental Pressure With a Note on Statistical Implications. Brit. Heart J. **6**: 176, 1944.

The casual blood pressure may be regarded as the sum of the basal blood pressure and the supplemental pressure; this last represents the degree of blood pressure elevation above the basal level due to whatever degree of physical, emotional, and suprabasal metabolic activity is present at the time of blood pressure measurement. The basal pressure is the pressure measured at a time when physical, emotional, and metabolic activity are reduced to a physiologic minimum. In cases where it is impossible to do this because of restlessness or emotional tension, the reading obtained should not be described as basal. Failure to obtain the true basal reading will not always be apparent to the observer especially when, as is most commonly the case, the failure is due to emotional reasons.

Both normal and hypertensive subjects with a high basal pressure have a greater statistical expectation of having a high casual pressure than do those whose basal pressure is low. Likewise those with high supplemental pressures have a greater statistical expectation of a high casual pressure than do those whose supplemental pressure is low.

In comparing one individual with another the basal and supplemental pressures are independent variables in the sense that the level of the basal blood pressure in an individual is no guide to the probable level of the supplemental pressure.

Most statistics concerning the level of the blood pressure are concerned with the casual readings. The fact that, when comparing one individual with another, within a comparable physiologic group, the casual blood pressure is to be regarded as the sum of two independent variables has statistical implications which are discussed.

The supplemental pressure forms a significantly higher proportion of the casual pressure among patients with essential hypertension than among normal subjects.

An improved method is recommended for determining the basal blood pressure.

AUTHOR.

Telford, I. R., Swegart, J. E., and Schoene, F. C.: Blood Pressure Studies on Normal and Vitamin E Deficient Rats. Am. J. Physiol. **143**: 214, 1945.

One-year-old vitamin E deficient female rats showed a reduction of 29 A per cent in their systolic blood pressure when compared with normal rats of the same age (78.2 mm. : 110.8 mm.). In 2-year-old vitamin E deficient rats the reduction in

blood pressure was essentially the same (29.2 per cent) as in the 1-year-old group. The systolic blood pressure for 2-year-old vitamin E deficient rats and normal control rats was 61.7 mm. and 87.2 mm., respectively. A lowering of the blood pressure in the second year of life is reflected equally in both experimental and control groups. This reduction is therefore due to an aging effect and is not a manifestation of a dietary deficiency. An histologic examination of the hearts and large vessels of vitamin E deficient rats failed to demonstrate any consistent vascular lesions that might contribute to a reduction of blood pressure. Variations in the room temperature, age and sex of the animal, and methods used in determining blood pressure are variables that influence the blood pressure readings in normal and experimental rats.

AUTHORS.

Quinby, W. C., Dexter, L., Sandmeyer, J. A., and Haynes, F. W.: The Renal Humoral Pressor Mechanism in Man. II. The Effect of Transitory Complete Constriction of the Human Renal Artery on Blood Pressure and on the Concentration of Renin, Hypertensinogen, and Hypertensinase of Renal Arterial and Venous Blood, With Animal Observations. J. Clin. Investigation 24: 69, 1945.

Complete constriction of the renal artery in five patients and in six dogs, for a period of twelve minutes, produced no rise in blood pressure after release of the clamp but did liberate small amounts of renin into the renal venous blood of the two patients in whom it was estimated and in two of six dogs.

In patients, the concentration of hypertensinogen was the same in the renal arterial and venous blood, before and after constriction of the renal artery, with one exception; hypertensinase, determined at a pH of 7.3 and 4.5, was likewise the same.

These observations demonstrate that by constriction of the renal artery in man, the renal humoral pressor mechanism is stimulated to activity as in animals.

AUTHORS.

Haynes, F. W., and Dexter, L.: The Renal Humoral Pressor Mechanism in Man. III. The Hypertensinase Content of Plasma of Control Subjects and of Patients With Hypertension and Other Diseases. J. Clin. Investigation 24: 75, 1945.

The hypertensinase content of nonhemolyzed plasma of ten normal subjects ranged from 1.1 to 1.8 dog units per milliliter of plasma. The hypertensinase content of the plasma of sixteen patients with hypertension, six patients with nitrogen retention, two patients with Addison's disease, and three patients with hepatic disease did not differ from the normal. It is concluded that there is no justification for considering that the blood pressure is high in human hypertension because of a deficiency of hypertensinase in plasma.

AUTHORS.

Grollman, A.: Experimental Chronic Hypertension in the Rabbit. Am. J. Physiol. 142: 666, 1944.

The blood pressure of adult rabbits was followed for three months or more following various operative procedures on the kidneys. The average rise in blood pressure following unilateral compression of the kidney did not exceed that which followed unilateral nephrectomy. Removal of the compressed kidney in a hypertensive animal did not result in lowering of the blood pressure. Rabbits may exhibit hypertension even in the absence of all renal tissue.

The implications of the observed results on the author's concept of the mechanism of experimental renal hypertension are discussed. In the rabbit, as in the rat, the available data support the view that chronic hypertension results from a deficiency induced by injury or removal of normal renal tissue and not from the formation of a renal pressor substance. The latter, however, may play a part in causing hypertension in the acute experiment.

AUTHOR.

Hueper, W. C.: Experimental Studies on the Therapy and the Prevention of Degenerative Vascular Diseases. II. The Effects of Several Detergents on Experimental Cholesterol Atheromatosis of Rabbits. Arch. Path. 38: 381, 1944.

Tergitol Penetrant 08 and Nacconol FSNO given by mouth elicited degenerative and calcifying lesions in the aortas of normal rabbits in addition to causing pulmonary edema, hyperemia and hemorrhages, and pleural effusion. Triton K-60 given by the same route did not produce any vascular reactions.

Similar pulmonary responses were seen in rabbits following repeated intravenous injections of Nacconol NRNO, while rabbits given injections of Triton NE exhibited marked irritation of the intestine. Rabbits into which Nacconol NRNO or Aerosol OT had been injected intravenously showed hyaline degenerated cerebral arteries and renal arterioles. Carcinomatoid proliferations were found in the lungs of rabbits fed Triton K-60 and Nacconol FSNO as well as in a cholesterolized rabbit given injections of Aerosol OT.

Following repeated oral administration of Aerosol OT, Triton NE and lithium iodide plus potassium thiocyanide in rabbits fed daily 0.5 Gm. of cholesterol in oil, it was noted that Aerosol OT seemed to interfere to some degree with the development of hypercholesteremia and atheromatosis, whereas Triton NE and lithium iodide plus potassium thiocyanide appeared to hasten and aggravate these processes.

Some of the evidence suggests that in certain respects there is an antagonism between the factors favoring atherosclerosis and those active in the production of thrombosis related to the wettability of the vascular wall, the circulatory conditions, and possibly also the oxygen-carbon dioxide tension of the blood.

AUTHOR.

Alberti, V. A. J., Segura, R. G., and Lanari, A.: Influence of Diminution of Intrathoracic Pressure on Blood Pressure in the Two Circulations. Medicina, Buenos Aires 5: 35, 1944.

The pressure changes in cats, with an endotracheal aspiration, were studied with regards to the aorta, the pulmonary artery, and both ventricles. The pressure readings were performed with Hamilton's manometer and through a thoracic puncture. The endothoracic depressions that occurred were about 30 cm. of water.

Negative pressures were registered in the pulmonary artery and in the right ventricle, without fall in the pulse pressure. The thoracic aortic pressure did not change, and, regarding the left ventricle, the systolic pressure was steady, while the diastolic was negative and similar to the right ventricle.

The etiology of these changes and their relationship to the pulmonary circulation in lung atelectasis are discussed.

AUTHORS.

Page, I. H., and Abell, R. G.: Effects of Acute Hemorrhage and of Subsequent Infusion Upon the Blood Vessels and Blood Flow as Seen in the Mesenteries of Anesthetized Dogs. Am. J. Physiol. 143: 182, 1945.

The method used in these experiments was to bleed the dogs acutely at short intervals until the pressure fell to 30 to 35 mm. Hg, and to maintain the animal in that state for thirty to forty-five minutes. Direct microscopic observations of the vessels in the mesentery of the dog showed that the arteries (0.39 to 1.2 mm. control diameters) constricted 20 to 60 per cent following removal of 2.5 to 5.5 per cent of the body weight of blood. The arterioles (24 to 65 diameters) usually constricted to a like degree, though sometimes slightly more. In many instances the larger veins (1 to 2.1 mm.) also constricted, the degree being from 12 to 43 per cent. The venules (160120) did not constrict; in some instances they dilated to 1.1 to 1.2 of their control diameters. The capillaries were not observed either to constrict or dilate. No measurements were made of arterioles having diameters of less than 24.

At hypotensive levels of about 30 mm. Hg, produced in these experiments by the removal of 3.5 to 5.5 per cent of the body weight of blood, the arterial flow was usually slow and pulsatile. Sometimes it was intermittent. Stasis was frequently present in some of the venules. For the most part the capillary bed was ischemic. Some variation occurred, however, and an occasional dog maintained a moderately

good flow even at this low level of pressure, whereas in some instances a sluggish flow was present in the mesenteries of some dogs even when the blood pressure was as high as 60 mm. of mercury.

Following such large hemorrhages, direct observations showed that the corpuscles in the vessels were separated by more than the normal amount of plasma. At arterial pressures of 30 to 40 mm. Hg, the intestine became bluish red, in contrast to its normal pink color during control periods.

Albumin infusions given into an artery after the pressure had been kept at 30 to 35 mm. Hg for half an hour restored the blood flow, caused the constricted arteries and arterioles to relax, the blood pressure to rise, and the intestine and tongue to return approximately to their normal colors. This was similar to the changes observed when the blood previously withdrawn was returned.

AUTHORS.

Baker, E. C., and Miller, F. A.: Further Experiences With Venography. Radiology **43**: 129, 1944.

The authors described a method of venography which, in their hands, has given practically complete visualization of the veins of the entire leg, thigh, and lower pelvis in most cases. The venograms are classified into types or patterns, indicating acute and chronic block of the superficial and of the deep plexuses. Three types of venous thrombosis have been observed and described. Four methods of abnormal venous return from the thigh to the body have been demonstrated. They believe that the procedure, when properly done, gives highly accurate information.

AUTHORS.

Jones, J. C., and Thompson, W. P.: Arteriovenous Fistula of the Lung. J. Thoracic Surg. **13**: 357, 1944.

Arteriovenous fistula of the lung produces a syndrome characterized by cyanosis, clubbing of fingers and toes, symptomatic polycythemia, and symptoms of anoxemia, usually in a young patient with an obscure lung tumor and a normal heart. A continuous murmur may be heard over the tumor.

The treatment is resection of the fistula or pulmonary resection, either of the lobe or the entire lung.

The case of a patient with arteriovenous fistula of the right lung cured by pneumonectomy is reported in detail.

AUTHORS.

Enikeeva, S. I.: The Mechanism of Epinephrine Bradycardia and Shock in Young Animals. Am. J. Physiol. **143**: 134, 1945.

Puppies less than 45 days old whose vagus centers show neither tonic activity nor reflex excitability respond with cardiac acceleration to small doses and cardiac slowing to large doses of epinephrine. Puppies and young rabbits show these responses after section of both vagi but the slowing does not occur after sympathectomy. Epinephrine bradycardia is through sympathetic innervation in very young animals.

Epinephrine bradycardia is reversible if the dose is not too large. If the dose exceeds the fatal dose for adults by eight to ten times, the young animal will die in thirty to one hundred eighty minutes. Death in two to four minutes, characteristic of the adult rabbit, occurs in the young rabbit only if the dose is twenty to thirty times the lethal dose for the adult.

Young rabbits do not show lung edema after epinephrine as do adults, though it may be produced in the young rabbit by lung irritants.

AUTHOR.

Rimmerman, A. B.: Digilanid and the Therapy of Congestive Heart Disease. Am. J. M. Sc. **209**: 33, 1945.

Digilanid, a complex of lanatosides A, B and C, the pure glycosides of *Digitalis lanata*, adjusted by weight, was studied in twenty-seven cases of congestive heart failure. Our investigation proves digilanid to be an effective cardio-active prepara-

tion, which has the advantages of purity, stability, and accuracy as to dosage and therapeutic effect.

The average oral digitalizing dose is 12⅞ mg. (thirty-eight tablets) while the oral maintenance dose was found to be ⅓ mg. (one tablet) in all but one case, which required ⅔ mg. (two tablets).

Digilanid intravenously in doses of 4 c.c. (2⅔ mg.) proves to be a potent therapeutic agent in congestive heart diseases with either normal rhythm or auricular fibrillation. The intravenous administration in doses of 4 c.c. is particularly indicated in cases of emergency, since its effect is reached within three hours, thus saving time of hospitalization.

AUTHOR.

Pines, I., Sanabria, A., and Arriens, R. T.: Mercurial Diuretics; The Addition of Magnesium Sulphate to Prevent the Toxic Effects of Their Intravenous Administration. Brit. Heart J. 6: 197, 1944.

The course of acute intoxication produced by the intravenous or intracardiac injections of esidrone was studied on normal dogs with the help of the electrocardiograph. It is concluded in agreement with other authors that mercurial diuretics in certain doses are general depressants for the whole cardiac muscle. The following pattern of intoxication was observed: changes of T waves, intraventricular and auriculo-ventricular conduction disturbances, diminution of frequency of impulse formation in S-A node, ventriuclar paroxysmal tachycardia, chaotic heart action, ventricular fibrillation, and death.

The addition of small quantities of magnesium sulfate (0.5 c.c. of a 20 per cent solution) prevents ventricular fibrillation and death, even if doses seven times higher than normal lethal doses are used. Magnesium sulfate, however, does not prevent, and even perhaps increases, the conduction disturbances resulting from the administration of lethal doses of mercurial diuretics. On the other hand, such amounts of magnesium sulfate increase the diuretic response, are entirely safe, and mix with mercurial diuretics without forming any precipitate.

It is suggested that small quantities of magnesium sulfate be incorporated into the mercurial diuretics in order to prevent fatal reactions resulting sometimes from the intravenous injections of these drugs.

AUTHOR.

Prescott, F.: Clinical Evaluation of the Pressor Activity of Methedrine, Neosynephrine, Paredrine, and Pholedrine. Brit. Heart J. 6: 214, 1944.

The clinical effectiveness of four pressor drugs, methedrine (pervitin, *d*-desoxyephedrine), paredrine, neosynephrin, and pholedrine (veritol, paredrinol) has been examined. Each drug was tested on twenty patients showing a severe fall in blood pressure (to 80 mm. Hg, systolic pressure, or to 10 mm. Hg, pulse pressure) during major surgical operations. The following were evaluated for each drug: optimum dose for a pressor response; maximum systolic and diastolic blood pressures, and rise in systolic and pulse pressuer after giving the drug; effect on pulse rate; time taken for the drug to act; duration of action; and side effects on the cardiovascular system. On the basis of the results obtained the clinical effectiveness of the four pressor drugs examined is in this order: methedrine, paredrine, neosynephrin, pholedrine. The principal criteria on which this opinion is based are: rise of systolic and pulse pressure when the drugs are given to surgical patients with a systolic blood pressure of 80 mm. Hg or less, the speed and duration of action, and the relative freedom from side effects on the cardiovascular system.

The table below summarizes the results obtained.

	Methedrine	Paredrine	Neosynephrin	Pholedrine
Satisfactory result	18	8	7	4
Unsatisfactory result	2	12	13	16
	20	20	20	20

A result was rated as satisfactory if the systolic pressure remained above 100 mm. Hg and the pulse pressure was not less than 30 mg. Hg for a period of two hours or more.

AUTHORS.

Book Reviews

THE FOETAL CIRCULATION AND CARDIOVASCULAR SYSTEM, AND THE CHANGES THAT THEY UNDERGO AT BIRTH. By Alfred E. Barclay, Kenneth J. Franklin, and Marjorie M. L. Prichard, Nuffield Institute for Medical Research, Oxford. Blackwell Scientific Publication, Ltd., Oxford, 1944, pp. xvi and 275, 160 illustrations, some in color; 50 shillings.

This monograph is a most interestingly written account of the fetal cardiovascular system and the circulation of the blood in one particular species of animals—the sheep—with a general discussion of this subject in other forms, especially in man. In it are brought together the results of a long series of painstaking experiments performed by a group of physiologists at Oxford, England, with the cooperation of their colleagues at Cambridge. It is definitely the most complete piece of work of its kind. The subject of the circulation through the heart of the fetus is a very old one. It is doubtful whether any subject in embryology has provoked so much discussion. Whether there is a separation or a complete mixing of the superior and inferior caval blood stream in the fetal right atrium is a question which has been thrown back and forth by investigators for at least three centuries. Here, for the first time, is a complete explanation of the true state of affairs in the fetal heart of one species of animals.

The first chapter of the monograph is an historical account divided into several periods. Much has been done to clarify certain misstatements which have been passed from one author to another in the literature. The second chapter of the book takes up the operative procedure and the special technique used to obtain roentgen cinematographic records. A detailed description is given of the special roentgenographic technique which was used to record the passage of contrast material through the heart and great vessels of the living fetus. Two types of recordings were used. In one of them a series of roentgenographic exposures was made on film 5 inches wide at the rate of three or four frames per second. The clearest images were produced by this method, but another, indirect method was found useful for obtaining records on 16 mm. motion picture film; an image on a fluorescent screen was photographed through a very fast lens.

The rest of the second chapter is devoted to a description of the results obtained by these methods—the actual course of the blood flow in the fetal lamb. Beautiful roentgenograms illustrate successive stages of the passage of radiopaque material through the vessels and heart in an adult animal (cat) and in the sheep fetus. In some experiments the contrast material reached the heart through the superior vena cava, and in others through the umbilical vein, ductus venosus, and inferior vena cava. The painstaking and detailed experiments which are described in this chapter of the book cannot be adequately covered in a review. One must read the authors' own account of these, and examine carefully their illustrations to fully appreciate the splendid results.

To summarize very briefly, they found that radiopaque material introduced through the superior caval stream passed through the right atrium, the right ventricle of the heart without traversing the foramen ovale, and entered the pulmonary trunk. A very appreciable amount went through the pulmonary circulation, and the rest of it was shunted by the ductus arteriosus into the descending aorta. Other experiments were performed to identify the ductus arteriosus definitely and to study the changes in the flow from the superior vena cava when the ductus arteriosus closed.

In an equally striking manner the authors demonstrated the course of radiopaque material traversing the inferior vena cava from the umbilical vein. It was found to pass very largely through the foramen ovale into the left atrium of the heart, the left ventricle, and thence through the arch of the aorta and the vessels to the heart itself, the upper extremities, and the head. A small fraction of the inferior caval stream traversed the right side of the heart, and thence went through the pulmonary circulation and ductus arteriosus.

Chapters III to VI are concerned with an attempt to tell the full anatomic and physiologic story of the cardiovascular system and circulation of the blood in the

mature sheep fetus and the changes which occeur during and after birth. Chapters VII and VIII deal with comparative anatomic and physiologic studies.

In the latter part of the book there are several chapters dealing with the cardiovascular system and changes occurring at human birth. Here the authors have brought together many widely scattered observations and have presented them in a most readable fashion.

The Foetal Circulation will be read with great interest by all who are concerned with the structure and function of the heart. It was a welcome surprise to learn of the publication of this book on a subject truly unrelated to the war, and in a country which has suffered so grievously in the present conflict. No small commendation to those responsible.

WILLIAM F. WINDLE.

EL APARATO CARDIOVASCULAR EN LAS INSUFICIENCIAS TIROIDEAS: By Dr. J. C. Mussio Fournier, Dr. José M. Cerviño, and Dr. Juan J. Bazzano. Salvat Editores, Barcelona and Buenos Aires, 1944, 150 pages, 27 illustrations.

This volume is published by the Institute of Endocrinology of the School of Medicine of Montevideo. The authors give a very complete review of the literature, together with the results of their study of sixty cases of myxedema.

Atherosclerosis, chronic renal lesions, myxedema heart disease, cardiac failure, angina pectoris, and myxedematous hydrops are discussed in the first part of the book as cardiovascular conditions which are directly due to myxedema.

The second part includes a discussion of cardiovascular disturbances caused by myxedema but superimposed on pre-existing lesions.

In the third part of the book there is a discussion of the transitory amelioration of either angina pectoris or cardiac failure which results from surgical removal of the thyroid gland.

In the last part the cardiovascular disturbances caused by thyroid treatment of myxedematous patients are considered.

The symptomatology of myxedema is studied systematically. Dyspnea, palpitation, precordial pain, mild peripheral edema, cyanosis, changes in cardiac rhythm and in arterial and venous pressure, and weakening of the heart sounds are critically considered. The two paragraphs on roentgenologic and electrocardiographic changes are of particular interest. The theory which attributes low voltage of the P and T waves to a change in the electrical resistance of the skin and that which attributes low voltage of QRS to the presence of fluid in the pericardial sac are discussed and held to be valid only in individual cases. Changes in the T wave and S-T segment can be ascribed directly to myxedema only when they fail to be modified by vasodilators and disappear during thyroid treatment.

Interstitial edema, in addition to separation and destruction of the myocardial fibers, is thought to be the main cause of the different signs of myocardial disease. Angina pectoris of myxedema which disappears after thyroid treatment is rare. It is attributed to underlying, silent coronary sclerosis, with superimposed functional elements either caused or favored by myxedema.

The discussion of the results of therapeutic thyroidectomy in cases of heart disease will be of interest to many cardiologists.

The photographs, roentgenograms, and electrocardiograms are well chosen and well reproduced, and the bibliography is complete.

A summary, with a brief statement of the authors' views on the different aspects of the subject, would have increased the value of the book, which will undoubtedly be read with interest.

ALDO LUISADA.

Announcement

In compliance with the order of the War Production Board, which limits the amount of paper consumed in the production of this JOURNAL, the publishers find it necessary to change the format. As soon as these restrictions are lifted the original format will be restored. Even though the number of pages has been reduced, the actual content of the JOURNAL has not been decreased to any appreciable extent.

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THE American Heart Association is the only national organization devoted to educational work relating to diseases of the heart. Its activities are under the control and guidance of a Board of Directors composed of thirty eminent physicians who represent every portion of the country.

A central office is maintained for the coordination and distribution of important information. From it there issues a steady stream of books, pamphlets, charts, films, lantern slides, and similar educational material concerned with the recognition, prevention, or treatment of diseases of the heart, which are now the leading cause of death in the United States. The American Heart Journal is under the editorial supervision of the Association.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning the circulation of blood and lymph. Any physician or investigator may become a member of the section after election to the American Heart Association and payment of dues to that organization.

The income from membership and donations provides the sole financial support of the Association. Lack of adequate funds seriously hampers more intensive educational activity and the support of important investigative work.

Annual membership is $5.00. Journal membership at $11.00 includes a year's subscription to the American Heart Journal (January-December) and annual membership in the Association. The Journal alone is $10.00 per year.

The Association earnestly solicits your support and suggestions for its work. Membership application blanks will be sent on request. Donations will be gratefully received and promptly acknowledged.